STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 111228

TO: Hong Liu **Location: CM1/4E01** **Art Unit: 1624** **Wednesday, January 07, 2004** **Case Serial Number: 09/678595**	**From: Barb O'Bryen** **Location: Biotech-Chem Library** **CM1-6A05** **Phone: 308-4291** **barbara.obryen@uspto.gov**

4E12

BOB

Search Notes

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=> fil reg; d stat que l16; fil capl; d que nos l18; fil uspatf; d que nos l19; dup rem
l18,l19
FILE 'REGISTRY' ENTERED AT 16:13:46 ON 07 JAN 2004
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STRUCTURE FILE UPDATES:    5 JAN 2004  HIGHEST RN 634558-38-6
DICTIONARY FILE UPDATES:   5 JAN 2004  HIGHEST RN 634558-38-6

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

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Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

L10      165325 SEA FILE=REGISTRY ABB=ON  16.239/RID
L11      371280 SEA FILE=REGISTRY ABB=ON  16.165/RID
L12      490595 SEA FILE=REGISTRY ABB=ON  46.383/RID
L13      567205 SEA FILE=REGISTRY ABB=ON  16.195/RID
L15         172 SEA FILE=REGISTRY ABB=ON  PT/ELS AND ((3/N AND (L11 OR L12 OR
                L13)) OR (2/N AND L10))
L16          52 SEA FILE=REGISTRY ABB=ON  L15 AND 1/NR

FILE 'CAPLUS' ENTERED AT 16:13:46 ON 07 JAN 2004
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FILE COVERS 1907 - 7 Jan 2004  VOL 140 ISS 2
FILE LAST UPDATED: 6 Jan 2004  (20040106/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L10      165325 SEA FILE=REGISTRY ABB=ON  16.239/RID
L11      371280 SEA FILE=REGISTRY ABB=ON  16.165/RID
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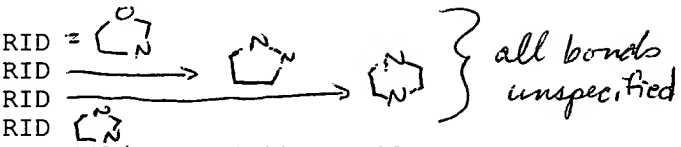

compound contains platinum

only 1 ring

```
L12      490595 SEA FILE=REGISTRY ABB=ON  46.383/RID
L13      567205 SEA FILE=REGISTRY ABB=ON  16.195/RID
L15         172 SEA FILE=REGISTRY ABB=ON  PT/ELS AND ((3/N AND (L11 OR L12 OR
                L13)) OR (2/N AND L10))
L16          52 SEA FILE=REGISTRY ABB=ON  L15 AND 1/NR
L18          25 SEA FILE=CAPLUS ABB=ON  L16


FILE 'USPATFULL' ENTERED AT 16:13:46 ON 07 JAN 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 6 Jan 2004 (20040106/PD)
FILE LAST UPDATED: 6 Jan 2004 (20040106/ED)
HIGHEST GRANTED PATENT NUMBER: US6675388
HIGHEST APPLICATION PUBLICATION NUMBER: US2004003444
CA INDEXING IS CURRENT THROUGH 6 Jan 2004 (20040106/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 6 Jan 2004 (20040106/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2003

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.


L10      165325 SEA FILE=REGISTRY ABB=ON  16.239/RID
L11      371280 SEA FILE=REGISTRY ABB=ON  16.165/RID
L12      490595 SEA FILE=REGISTRY ABB=ON  46.383/RID
L13      567205 SEA FILE=REGISTRY ABB=ON  16.195/RID
L15         172 SEA FILE=REGISTRY ABB=ON  PT/ELS AND ((3/N AND (L11 OR L12 OR
                L13)) OR (2/N AND L10))
L16          52 SEA FILE=REGISTRY ABB=ON  L15 AND 1/NR
L19           1 SEA FILE=USPATFULL ABB=ON  L16


FILE 'CAPLUS' ENTERED AT 16:13:46 ON 07 JAN 2004
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FILE 'USPATFULL' ENTERED AT 16:13:46 ON 07 JAN 2004
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PROCESSING COMPLETED FOR L18
PROCESSING COMPLETED FOR L19
L21 26 DUP REM L18 L19 (0 DUPLICATES REMOVED)
ANSWERS '1-25' FROM FILE CAPLUS
ANSWER '26' FROM FILE USPATFULL

=> d ibib abs hitstr 1-26; fil cao; d que nos l20

L21 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173417 CAPLUS
DOCUMENT NUMBER: 138:214473
TITLE: Platinum complexes containing nonplanar heterocyclic aliph. amines and their use in cancer treatment
INVENTOR(S): Barenholz, Yechezkel; Gibson, Dan; Najajreh, Yousef; Khazanov, Elena
PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003017998	A1	20030306	WO 2002-IL687	20020821
WO 2003017998	B1	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-314115P P 20010823
OTHER SOURCE(S): MARPAT 138:214473

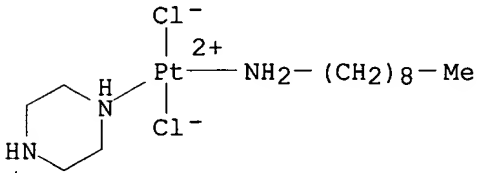
AB The present invention concerns novel Pt complexes in which at least one of the amine ligands is a nonplanar heterocyclic aliph. amine. Claimed are platinum complexes [Pt(X)(Y)(Am1)(Am2)] [X and Y = halo, carboxylate, phosphate, or sulfate; Am1 = amine selected from NH3, primary amine, secondary amine, non-planar heterocyclic aliph. amine or heterocyclic arom. amine; Am2 = non-planar heterocyclic aliph. amine, with the proviso that when said complex has cis configuration, Am1 and Am2 cannot represent simultaneously piperidine] and their pharmaceutical compns. Prepd. claimed complexes include trans-[PtCl2(NH3)(Am2)] (Am2 = piperidine, 4-hydroxypiperidine, 4-piperidinopiperidine, etc.), cis-[PtCl2(NH3)(piperidine)] or cis-[PtCl2(NH3)(piperazine)].cntdot.HCl, and linked dinuclear complex bis[{trans,trans-PtCl2(piperazine)2}{4,7,10-trioxo-1,13-tridecanediamine}].cntdot.2HCl. The Pt complexes may be in a trans or cis configuration and possess therapeutic antitumor activities. Achieving a therapeutic effect may comprise forming an adduct between the Pt complex and DNA, inducing apoptosis of undesired cell proliferation, and loading the Pt complex into a liposome. Cytotoxicity assays revealed that replacing one or both ammines of transplatin enhanced significantly the cytotoxicity of the trans-PtCl2 compds. in both human C-26 colon and human OV-1063 ovarian cancer cell lines. Improved antitumor activity was detd. for piperidine- and piperazine-contg. platinum complexes against resistance cancer cell lines A2780/A2780cisR, 41M/41McisR, and

CH1/CH1cisR.

IT **499769-13-0P 499769-14-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. as antitumor agent)

RN 499769-13-0 CAPLUS

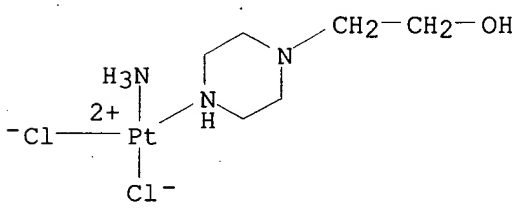
CN Platinum, dichloro(1-nonanamine)(piperazine-.kappa.N1)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)



● HCl

RN 499769-14-1 CAPLUS

CN Platinum, amminedichloro(1-piperazineethanol-.kappa.N4)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)

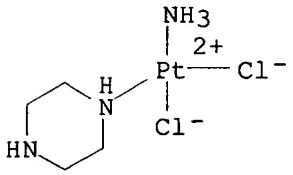


● HCl

IT **499982-35-3P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. as antitumor agent and DNA binding)

RN 499982-35-3 CAPLUS

CN Platinum, amminedichloro(piperazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

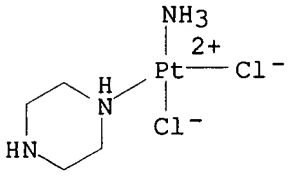


IT **478844-04-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. as antitumor agent and activity against C-26 colon and OV-1063 ovarian cancer cell lines and resistance cancer cell lines A2780/A2780cisR, 41M/41McisR, and CH1/CH1cisR)

RN 478844-04-1 CAPLUS

CN Platinum, amminedichloro(piperazine-.kappa.N1)-, monohydrochloride, (SP-4-2)- (9CI) (CA INDEX NAME)



● HCl

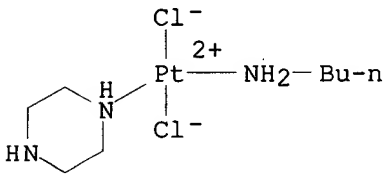
IT **478842-92-1P 478843-07-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. as antitumor agent and activity against resistance cancer cell lines A2780/A2780cisR, 41M/41McisR, and CH1/CH1cisR)

RN 478842-92-1 CAPLUS

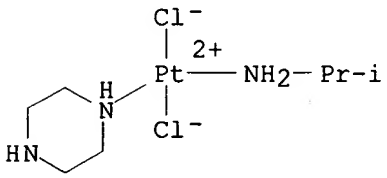
CN Platinum, (1-butanamine)dichloro(piperazine-.kappa.N1)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)



● HCl

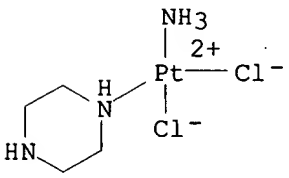
RN 478843-07-1 CAPLUS

CN Platinum, dichloro(piperazine-.kappa.N1)(2-propanamine)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)



● HCl

IT **478842-82-9P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. as antitumor agent, activity against resistance cancer cell lines A2780/A2780cisR, 41M/41McisR, and CH1/CH1cisR, and DNA binding)
RN 478842-82-9 CAPLUS
CN Platinum, amminedichloro(piperazine-.kappa.N1)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)



● HCl

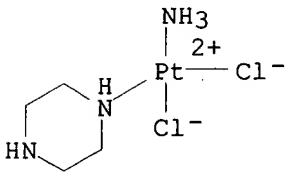
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:326574 CAPLUS
DOCUMENT NUMBER: 139:62614
TITLE: DNA Binding Mode of the Cis and Trans Geometries of New Antitumor Nonclassical Platinum Complexes Containing Piperidine, Piperazine, or 4-Picoline Ligand in Cell-Free Media. Relations to Their Activity in Cancer Cell Lines
AUTHOR(S): Kasparkova, Jana; Marini, Victoria; Najajreh, Yousef; Gibson, Dan; Brabec, Viktor
CORPORATE SOURCE: Institute of Biophysics, Academy of Sciences of the Czech Republic, Brno, CZ-61265, Czech Rep.
SOURCE: Biochemistry (2003), 42(20), 6321-6332
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The global modification of mammalian and plasmid DNAs by novel platinum compds., cis- or trans-[PtCl2(NH3)(Am)], where Am = NH3, nonplanar heterocycle piperidine, piperazine, or arom. planar heterocycle 4-picoline, was investigated in cell-free media using various biochem. and biophys. methods. These modifications have been compared with the activity of these new compds. in several tumor cell lines including those resistant to antitumor cis-diamminedichloroplatinum(II) (cisplatin). The results show that the replacement of the NH3 group in cisplatin by the heterocyclic ligands does not considerably affect the DNA binding mode of this drug. Cytotoxicity studies have revealed that the replacement lowers the activity of the platinum compd. in both sensitive and resistant cell lines. It has been suggested that the reduced activity of these analogs of cisplatin is assocd. with some features of the damaged DNA and/or its cellular processing. Alternatively, the reduced activity of the analogs of cisplatin might also be due to the factors that do not operate directly at the level of the target DNA, such as intracellular platinum uptake. In contrast to the analogs of cisplatin, the replacement of one ammine group by the heterocyclic ligand in its clin. ineffective trans isomer (transplatin) results in a radical enhancement of its activity in tumor

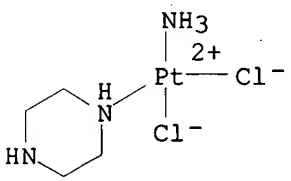
cell lines. Importantly, this replacement also markedly alters the DNA binding mode of transplatin. The results support the view that one strategy of how to activate the trans geometry in bifunctional platinum(II) compds. including circumvention of resistance to cisplatin may consist of a chem. modification of the ineffective transplatin that results in an increased stability of its intrastrand cross-links in double-helical DNA and/or in an increased efficiency to form interstrand cross-links.

IT **499982-35-3 548446-31-7**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DNA binding mode of cis and trans antitumor nonclassical platinum complexes contg. piperidine and piperazine and 4-picoline ligands in relation to antitumor activity and resistance)

RN 499982-35-3 CAPLUS
CN Platinum, amminedichloro(piperazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 548446-31-7 CAPLUS
CN Platinum, amminedichloro(piperazine-.kappa.N1)-, (SP-4-1)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

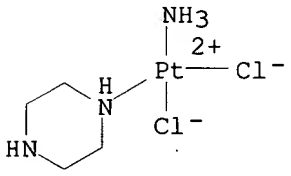
L21 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:913261 CAPLUS
DOCUMENT NUMBER: 138:364333
TITLE: Ligand effects on the binding of cis- and trans-[PtCl2Am1Am2] to proteins
AUTHOR(S): Najajreh, Yousef; Peleg-Shulman, Tal; Moshel, Ofra; Farrell, Nicholas; Gibson, Dan
CORPORATE SOURCE: School of Pharmacy, Department of Medicinal Chemistry and Natural Products, The Hebrew University of Jerusalem, Jerusalem, 91120, Israel
SOURCE: JBIC, Journal of Biological Inorganic Chemistry (2003), 8(1-2), 167-175
CODEN: JJBCFA; ISSN: 0949-8257
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As part of a systematic study of the basic principles that govern the formation and reactivity of Pt-protein adducts, we report the effect of substituting the ammine ligand of cis- and trans-[PtCl2(NH3)2] complexes with bulkier planar arom. or nonplanar cyclic amine ligands on the binding

properties of the complexes to ubiquitin and to horse heart myoglobin. The ligand replacement had a different effect on the cis or trans isomers investigated. In the cis-Pt complexes, replacing one or both ammine ligands by piperidine or 4-picoline dramatically decreased the binding of the complexes to the proteins studied, whereas in the substituted trans-Pt complexes replacement of the ammine by a piperidine or 4-picoline increased the binding rate. This behavior may have to do with the different preferred binding sites of the cis- and trans-Pt complexes. The bulkier cis- or trans-Pt complexes investigated also did not display a preference for Met1 of ubiquitin, possibly owing to steric constraints imposed by the substituted ligands. The introduction of a charged piperazine ligand significantly decreased the rate of binding to the protein, possibly owing to electrostatic interactions or hydrogen-bond formations with the surface of the protein. The binding of the complexes to ubiquitin and myoglobin does not disrupt the folding of the proteins as judged by electrospray ionization mass spectrometry.

IT **478842-82-9P**
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(ligand effects on binding of cis- and trans-[PtCl2Am1Am2] to proteins)

RN 478842-82-9 CAPLUS
CN Platinum, amminedichloro(piperazine-.kappa.N1)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:275998 CAPLUS
DOCUMENT NUMBER: 136:288219
TITLE: Platinum ammine complexes or derivatives with improved aqueous solubility and activity as antitumor agents
INVENTOR(S): Wong, Ernest S. Y.; Giandomenico, Christen M.
PATENT ASSIGNEE(S): Anormed Inc., Can.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028871	A1	20020411	WO 2001-US30838	20011002

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001094969	A5	20020415	AU 2001-94969		20011002
EP 1322654	A1	20030702	EP 2001-975671		20011002
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PRIORITY APPLN. INFO.:			US 2000-678595	A	20001004
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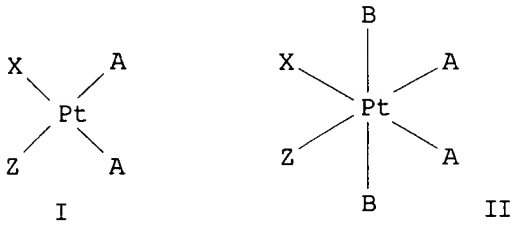
GI

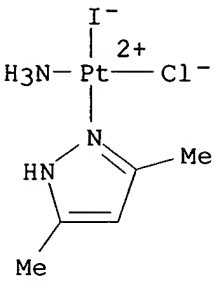


AB The present invention relates to Pt antitumor drugs. In particular, it relates to Pt complexes I or II or a pharmaceutically acceptable salt thereof wherein each A is independently an anion, each B is independently halo, hydroxy, carboxylate, carbamate or a carbonate ester, Z is a substituted 5- or 6-membered, heterocyclic moiety wherein at least one substituent sterically hinders access of the Pt atom to a DNA strand of a tumor cell, and wherein Z is other than pyridine, and X is NH3 or mono- or dialkyl-substituted NH3, which are active against human cancer cells and have improved aq. soly. and activity. Example complexes which are prepd. include cis-[PtII(NH3)Cl2(L)] (L = 3,5-dimethylpyrazole, 1-methylimidazole, 3,5-dimethylisoxazole, 2,3-dimethylpyrazine, etc.) or (OC-6-43)-[PtIV(NH3)Cl2(OH)2(L)] (L = 3,5-dimethylpyrazole, 1-methylimidazole, 2,3-dimethylpyrazine) or (OC-6-43)-[PtIV(NH3)Cl2(OAc)2(L)] (L = 2,3-dimethylpyrazine). The aq. soly. of the complexes at ambient conditions are greater than that of cisplatin. The activity of the complexes in inhibiting human cell lines is comparable to that of prior art compds., at least in some cell lines. Resistance factors with respect to 41M/41MR are particularly favorable for some of the complexes.

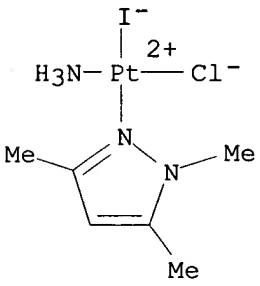
IT **406161-68-0P 406161-69-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; for prepn. of amminedichloro(N-heterocycle)platinum(II) complex)

RN 406161-68-0 CAPLUS

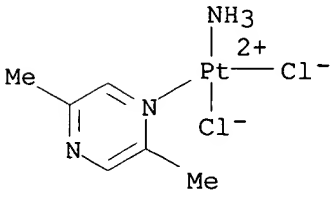
CN Platinum, amminechloro(3,5-dimethyl-1H-pyrazole-.kappa.N2)iodo- (9CI) (CA INDEX NAME)



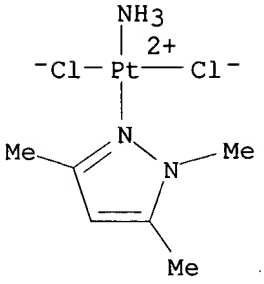
RN 406161-69-1 CAPLUS
CN Platinum, amminechloroiodo(1,3,5-trimethyl-1H-pyrazole-.kappa.N2)- (9CI) (CA INDEX NAME)



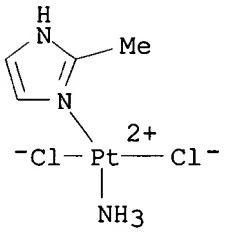
IT **301299-27-4P 406161-57-7P 406161-60-2P**
406161-62-4P 406161-63-5P 406161-64-6P
406161-65-7P 406161-66-8P 406161-67-9P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., aq. soly., and antitumor activity)
RN 301299-27-4 CAPLUS
CN Platinum, amminedichloro(2,5-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



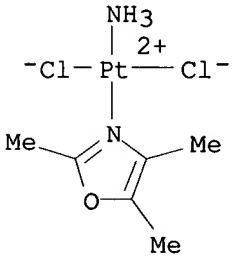
RN 406161-57-7 CAPLUS
CN Platinum, amminedichloro(1,3,5-trimethyl-1H-pyrazole-.kappa.N2)-, (SP-4-3)- (9CI) (CA INDEX NAME)



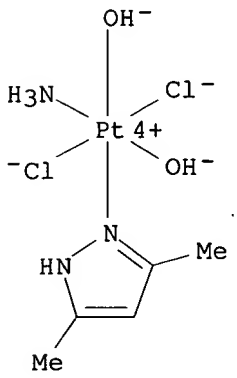
RN 406161-60-2 CAPLUS
CN Platinum, amminedichloro(2-methyl-1H-imidazole-.kappa.N3)-, (SP-4-3)-(9CI) (CA INDEX NAME)



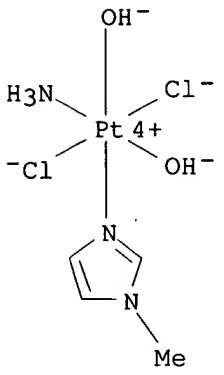
RN 406161-62-4 CAPLUS
CN Platinum, amminedichloro(trimethyloxazole-.kappa.N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



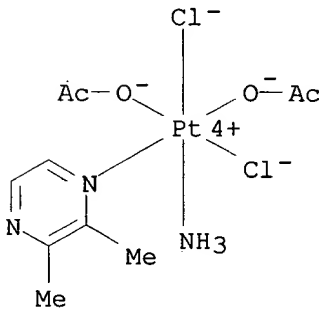
RN 406161-63-5 CAPLUS
CN Platinum, amminedichloro(3,5-dimethyl-1H-pyrazole-.kappa.N2)dihydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)



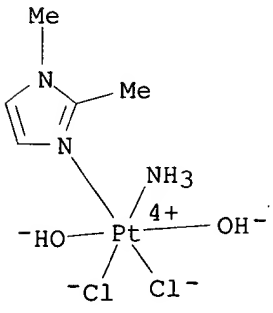
RN 406161-64-6 CAPLUS
CN Platinum, amminedichlorodihydroxy(1-methyl-1H-imidazole-.kappa.N3)-, (OC-6-43)- (9CI) (CA INDEX NAME)



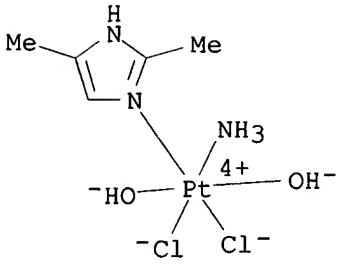
RN 406161-65-7 CAPLUS
CN Platinum, bis(acetato-.kappa.O)amminedichloro(2,3-dimethylpyrazine-.kappa.N1)-, (OC-6-43)- (9CI) (CA INDEX NAME)



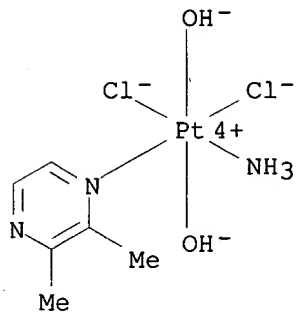
RN 406161-66-8 CAPLUS
CN Platinum, amminedichloro(1,2-dimethyl-1H-imidazole-.kappa.N3)dihydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)



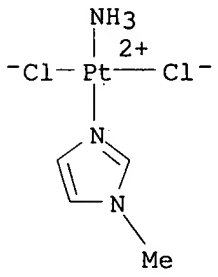
RN 406161-67-9 CAPLUS
CN Platinum, amminedichloro(2,5-dimethyl-1H-imidazole-.kappa.N3)dihydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)



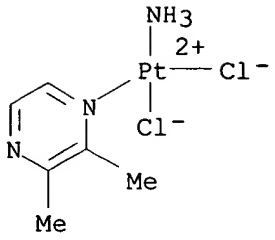
IT **301299-34-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn., conversion to diacetato deriv., and use as antitumor agent)
RN 301299-34-3 CAPLUS
CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)dihydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)



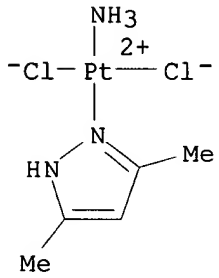
IT **114487-38-6P 301299-38-7P 406161-56-6P 406161-59-9P 406161-61-3P**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn., peroxide oxidn. to dihydroxo deriv., aq. soly., and antitumor activity)
RN 114487-38-6 CAPLUS
CN Platinum, amminedichloro(1-methyl-1H-imidazole-.kappa.N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



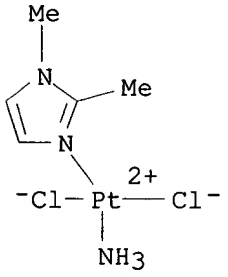
RN 301299-38-7 CAPLUS
CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



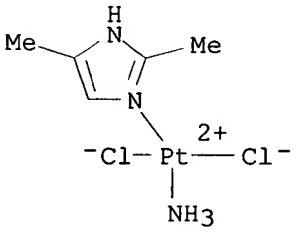
RN 406161-56-6 CAPLUS
CN Platinum, amminedichloro(3,5-dimethyl-1H-pyrazole-.kappa.N2)-, (SP-4-3)-
(9CI) (CA INDEX NAME)



RN 406161-59-9 CAPLUS
CN Platinum, amminedichloro(1,2-dimethyl-1H-imidazole-.kappa.N3)-, (SP-4-3)-
(9CI) (CA INDEX NAME)



RN 406161-61-3 CAPLUS
CN Platinum, amminedichloro(2,5-dimethyl-1H-imidazole-.kappa.N3)-, (SP-4-3)-
(9CI) (CA INDEX NAME)



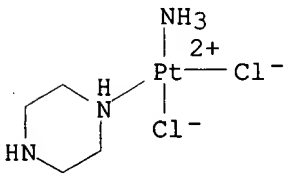
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:830840 CAPLUS
DOCUMENT NUMBER: 138:32969
TITLE: Novel Soluble Cationic trans-Diaminedichloroplatinum(II) Complexes that Are Active against Cisplatin Resistant Ovarian Cancer Cell Lines
AUTHOR(S): Najajreh, Yousef; Perez, Jose Manuel; Navarro-Ranninger, Carmen; Gibson, Dan
CORPORATE SOURCE: Department of Medicinal Chemistry and Natural Products, School of Pharmacy, The Hebrew University of Jerusalem, Jerusalem, 91120, Israel
SOURCE: Journal of Medicinal Chemistry (2002), 45(24), 5189-5195
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pos. charged, water sol. cis/trans-[PtCl2(piperazine)(Am1)] (where Am1 = NH3, n-butylamine, isopropylamine, 4-picoline, piperidine, and piperazine) has significant cytotoxic activity against cisplatin resistant ovarian cancer cells. The charged complexes are taken up by cancer cells much more rapidly than cisplatin and bind to cellular DNA and to calf thymus DNA much faster than cisplatin or transplatin. The platinum-piperazine complexes bind proteins (ubiquitin and myoglobin) very slowly as compared to cisplatin and to their neutral piperidine analogs. Altogether, the results reported here suggest that combination of pos. charged ligands with a trans-Pt(II)Cl center may lead to the discovery of platinum complexes that are able to circumvent cisplatin resistance.

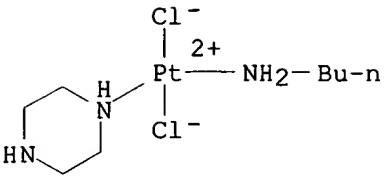
IT **478842-82-9P 478842-92-1P 478843-07-1P 478844-04-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor aminedichloroplatinum complexes active against cisplatin resistant ovarian cancer cell lines)

RN 478842-82-9 CAPLUS
CN Platinum, amminedichloro(piperazine-.kappa.N1)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)



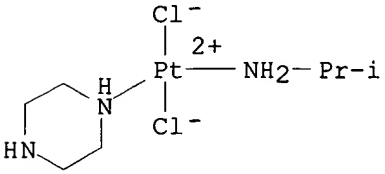
● HCl

RN 478842-92-1 CAPLUS
CN Platinum, (1-butanamine)dichloro(piperazine-.kappa.N1)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)



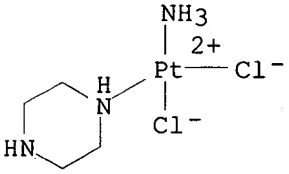
● HCl

RN 478843-07-1 CAPLUS
CN Platinum, dichloro(piperazine-.kappa.N1)(2-propanamine)-, monohydrochloride, (SP-4-1)- (9CI) (CA INDEX NAME)



● HCl

RN 478844-04-1 CAPLUS
CN Platinum, amminedichloro(piperazine-.kappa.N1)-, monohydrochloride, (SP-4-2)- (9CI) (CA INDEX NAME)



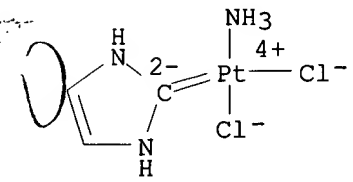
● HCl

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

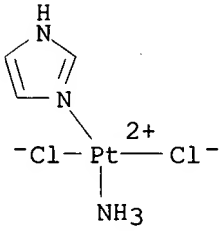
L21 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:918107 CAPLUS
DOCUMENT NUMBER: 136:200291
TITLE: Preferential C-Binding versus N-Binding in Imidazole Depends on the Metal Fragment Involved
AUTHOR(S): Sini, Gjergji; Eisenstein, Odile; Crabtree, Robert H.
CORPORATE SOURCE: Universite de Cergy-Pontoise, Cergy-Pontoise, 95031, Fr.
SOURCE: Inorganic Chemistry (2002), 41(3), 602-604
CODEN: INOCAJ; ISSN: 0020-1669

Searched by Barb O'Bryen, STIC 308-4291

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The relative stability of metal fragment involved imidazole C- and N-bound isomers is discussed. The position of equil., where N-bound imidazole rearranges to the C-bound form, with the proton originally bound to the 2-carbon moving to nitrogen, is discussed. C-bound imidazoles are predicted to be thermodynamically more stable than the conventional N-bound forms for several second- and third-row transition metals.
IT **400900-34-7 401815-12-1**
RL: PRP (Properties)
(relative energy; preferential C-binding vs. N-binding in imidazole depends on metal fragment involved)
RN 400900-34-7 CAPLUS
CN Platinum, amminedichloro(1,3-dihydro-2H-imidazol-2-ylidene)-, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 401815-12-1 CAPLUS
CN Platinum, amminedichloro(1H-imidazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:742103 CAPLUS
DOCUMENT NUMBER: 133:304927
TITLE: Process for preparing amine platinum complexes
INVENTOR(S): Wong, Ernest S. Y.; Giandomenico, Christen M.
PATENT ASSIGNEE(S): Anormed, Inc., Can.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061590	A1	20001019	WO 2000-CA385	20000411

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,

LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000009780	A	20020102	BR 2000-9780	20000411
EP 1165576	A1	20020102	EP 2000-918620	20000411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541263	T2	20021203	JP 2000-610861	20000411
EE 200100536	A	20030217	EE 2001-536	20000411
ZA 2001007965	A	20030102	ZA 2001-7965	20010927
NO 2001004957	A	20011203	NO 2001-4957	20011012
BG 106090	A	20020628	BG 2001-106090	20011108

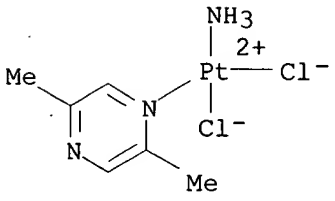
PRIORITY APPLN. INFO.: US 1999-128939P P 19990413
WO 2000-CA385 W 20000411

OTHER SOURCE(S): MARPAT 133:304927

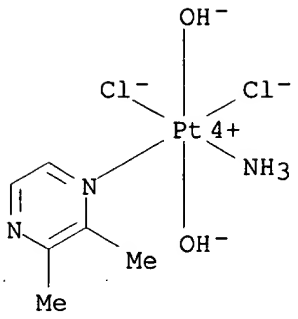
AB The present invention relates to the area of Pt amine drugs. In particular, it relates to an improved process for prepg. Pt complexes PtA2LL1 (Ia) or PtA2Y2LL1 (Ib), comprising: (1a) a 1st step, wherein [PtA4]2-, preferably PtCl42-, is reacted with L under appropriate conditions in a 1st solvent to form [PtA3(L)]-; (1b) a 2nd step, wherein [PtA3(L)]- is reacted with L' under appropriate conditions in a 2nd solvent to form cis-[PtA2(L')(L)]; (1c) in the case there Y is halogen or hydroxy a third step, wherein cis-[PtA2(L')(L)] is reacted with H2O2, Y2 or halogen contg. oxidant to form c,t,c-[PtA2Y2(L')(L)]; in the case where Y is carboxylate, carbamate or carbonate ester a 4th step, wherein an intermediate, where Y is hydroxy formed in step (1c), is functionalized with an appropriate acylating agent; and (1d) in the case where A is not a halide or is different from the original halide, addnl. step(s) in which the original halide A of an intermediate formed in step 1a or 1b, 1c or 1d is converted to a different halide or a new leaving group(s) A such as mono-dentate hydroxy, alkoxy, carboxylate or bidentate carboxylate, phosphonocarboxylate, diphosphonate, or sulfate; wherein L = amine or NH3, L' = amine but not NH3 and Y is a halogen, hydroxide, carboxylate, carbamate or carbonate ester. For example, K2[PtCl4] in N-methylpyrrolidinone reacted with 2-picoline (pic) to give K[PtCl3L] which in aq. soln. in presence of KCl reacted with NH4OAc in presence of NH4OH to give [PtCl2(NH3)(pic)]. [PtCl2(NH3)(pic)] was oxidized by H2O2 to give to give cis,trans,cis-[PtCl2(OH)2(NH3)(pic)] which was converted to [PtCl(OH)3(NH3)(pic)] and subsequently to [PtCl(OAc)3(NH3)(pic)].

IT **301299-27-4P 301299-34-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(improved prepn. of antitumor agent)

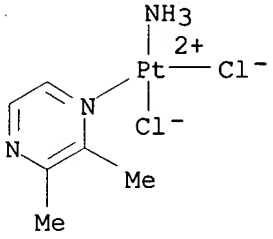
RN 301299-27-4 CAPLUS
CN Platinum, amminedichloro(2,5-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 301299-34-3 CAPLUS
CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)dihydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)



IT **301299-38-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for improved prepn. of platinum amine complexes as antitumor agents)
RN 301299-38-7 CAPLUS
CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:558981 CAPLUS
DOCUMENT NUMBER: 129:297999
TITLE: In vitro and in vivo activity of two Pt(IV) salts against Leishmania donovani
AUTHOR(S): Mesa-Valle, C. M.; Rodriguez-Cabezas, M. N.; Moraleda-Lindez, V.; Craciunescu, D.; Sanchez-Moreno, M.; Osuna, A.
CORPORATE SOURCE: Departamento Biologia Aplicada, Facultad Ciencias Experimentales, Universidad Almeria, Almeria, Spain
SOURCE: Pharmacology (1998), 57(3), 160-172
CODEN: PHMGBN; ISSN: 0031-7012
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The activities of 8 Pt drug complex salts were detd. against L. donovani promastigotes. The 3 most active salts were selected: [PtIVBr6]H2 (pentamidine), [PtIVBr6]H2 (stilbamidine), and [PtIVCl6]H2 (2-piperazinyl(1) Et amine), which induced growth-inhibition rates of >50% at 24 h of treatment and at the max. dosage tested. The cytotoxicity assays on the macrophage cell line J-774 showed high cytotoxicity for the salt [PtIVBr6]H2 (stilbamidine) with a percentage of specific 51Cr release of 58.2% at 24 h of incubation and 100 .mu.g/mL. Meanwhile, assays of the other compds. showed practically no cytotoxicity. The salt [PtIVBr6]H2 (pentamidine) notably inhibited the incorporation of 3H-thymidine in the treated parasites. The ultrastructural alterations obsd. in the flagellates treated with the salts [PtIVCl6]H2 (2-piperazinyl(1)Et amine)

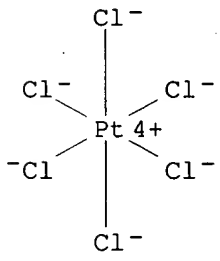
and [PtIVBr6]H2 (pentamidine) suggest that both act preferentially at the nuclear level and at the kinetoplast-mitochondrion complex. Both compds. showed a high in vivo activity in parasitized Wistar rats.

IT **66098-32-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiparasitic activity of Pt(IV) salts)

RN 66098-32-6 CAPLUS
CN Platinate(2-), hexachloro-, (OC-6-11)-, dihydrogen, compd. with 1-piperazineethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

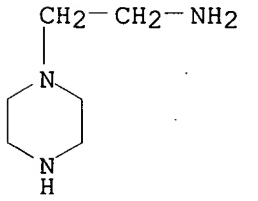
CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS



2 H^+

CM 2

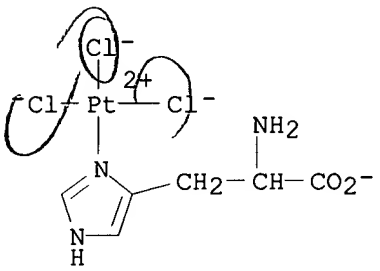
CRN 140-31-8
CMF C6 H15 N3



L21 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:254588 CAPLUS
DOCUMENT NUMBER: 122:70654
TITLE: Monohistidine complexes of platinum(II) and palladium(II)
AUTHOR(S): Krylova, L. F.; Dikanskaya, L. D.; Fedotov, M. A.
CORPORATE SOURCE: Novosib. Gos. Univ., Russia
SOURCE: Koordinatsionnaya Khimiya (1994), 20(10), 780-5
CODEN: KOKHDC; ISSN: 0132-344X
PUBLISHER: MAIK Nauka
DOCUMENT TYPE: Journal

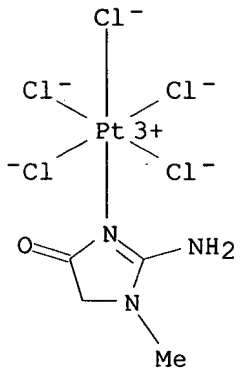
Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE: Russian
AB K2MCl4 (M = Pt, Pd) reacted with histidine (HL) in a 1:1 ratio in aq. soln. to give [MLCl(H2O)] (I), [Pt(HL)Cl2] (II), [Pt(H2L)Cl3] (III) and H3L[MCl4]. The complexes were characterized by 1H, 14N and 195Pt NMR and IR spectra. I are mixts. of complexes of the same compn., contg. tautomeric forms of L-. For I (M = Pd) the mixt. was sepd. The mode of coordination of HL in II is analogous to that found in the Pd analog. In III H2L+ is coordinated through the tertiary N of the heterocycle.
IT **160208-88-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 160208-88-8 CAPLUS
CN Platinate(2-), trichloro(L-histidinato-N3)-, dihydrogen, (SP-4-2)- (9CI) (CA INDEX NAME)



●2 H^+

L21 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:21466 CAPLUS
DOCUMENT NUMBER: 122:92534
TITLE: Photochemistry of PtCl62- complex and reactions of intermediate Pt(III) complexes with bioorganic ligands
AUTHOR(S): Plyusnin, V. F.; Grivin, V. P.
CORPORATE SOURCE: Inst. Khim. Kinet. Goren., Novoskbirsk, 630090, Russia
SOURCE: Khimiya Vysokikh Energii (1994), 28(3), 252-6
CODEN: KHVKAO; ISSN: 0023-1193
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Spectral and kinetic characteristics were detd. of the transient Pt(III) complexes produced in laser photolysis of PtCl62- in alc. solns. Unstability of the coordination sphere of the Pt(III) ion allows to utilize photochem. of PtCl62- for a fast synthesis of the new coordination compds. of Pt(II). Bioorg. ligands (L) react fast with transient PtCl52- to form PtCl52-...L. In many cases the ligands remained in the coordination sphere during Pt(III) .fwdarw. Pt(II) transformation, what led to photochem. synthesis of Pt(II) compds.
IT **128507-00-6P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(photochem. of PtCl62- complex and reactions of intermediate Pt(III) complexes with creatinine)
RN 128507-00-6 CAPLUS
CN Platinate(2-), (2-amino-1,5-dihydro-1-methyl-4H-imidazol-4-one-N3)pentachloro-, (OC-6-21)- (9CI) (CA INDEX NAME)

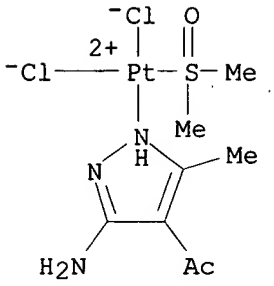


L21 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:182038 CAPLUS
DOCUMENT NUMBER: 118:182038
TITLE: Dehydrohalogenation and dimeric complex formation proceeded at the solid-phase heating of trans-[Pt(3-methyl-4-acetyl-5-aminopyrazole)(dimethyl sulfoxide)Cl2]. X-ray structure of the di-.mu.-N1,N2-(3-methyl-4-acetyl-5-aminopyrazolate)bis(dimethyl sulfoxide)dichlorodiplatinum(II)
AUTHOR(S): Kukushkin, V. Yu.; Aleksandrova, E. A.; Leovac, Vukadin, M.; Iveges, Erika Z.; Belsky, Vitalii K.; Konovalov, Vadim E.
CORPORATE SOURCE: Dep. Chem., St. Petersburg State Univ., Stary Petergof, 198904, Russia
SOURCE: Polyhedron (1992), 11(20), 2691-6
CODEN: PLYHDE; ISSN: 0277-5387
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The bridge-splitting reaction of [Pt(Me2SO)(.mu.-Cl)Cl]2 with 3-methyl-4-acetyl-5-aminopyrazole (R3PzH) in acetone gives trans-[Pt(Me2SO)(R3PzH)Cl2] (I). On heating in the solid phase I undergoes thermal conversion to give [Pt2(R3Pz)2(Me2SO)2Cl2] (II) and the abstraction of HCl. The structure of II was detd. by x-ray diffraction anal. The complex exhibits a heat-to-tail dimeric structure with 2 bridged pyrazolate anions. The dimerization reaction represents an unusual type of solid-phase conversion of Pt complexes, which can be considered as a variant of the Anderson rearrangement. I and II were also characterized by elemental anal., IR spectral and TGA (I only) methods.

IT **147020-61-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and solid-state dimerization of)

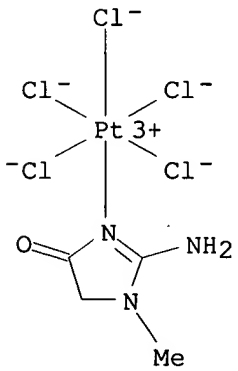
RN 147020-61-9 CAPLUS
CN Platinum, [1-(3-amino-5-methyl-1H-pyrazol-4-yl)ethanone]dichloro[sulfinylbis[methane]-S]-, (SP-4-1)- (9CI) (CA INDEX NAME)



L21 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:488018 CAPLUS
DOCUMENT NUMBER: 113:88018
TITLE: Pulsed laser photolysis of the hexachloroplatinate (PtCl62-)-creatinine system in methanol
AUTHOR(S): Grivin, V. P.; Plyusnin, V. F.; Khmelinski, I. V.; Bazhin, N. M.; Mitewa, M.; Bontchev, P. R.
CORPORATE SOURCE: Inst. Chem. Kinet. Combust., Novosibirsk, 630 090, USSR
SOURCE: Journal of Photochemistry and Photobiology, A: Chemistry (1990), 51(3), 371-7
CODEN: JPPCEJ; ISSN: 1010-6030
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pulsed laser photolysis (excimer laser, XeCl; 308 nm) of the PtCl62--creatinine-methanol system was studied. The formation of an intermediate PtIII species (PtCl52--cr, where cr = creatinine) was demonstrated and its decay kinetics were examd. Some kinetic and thermodn. data of the photoinduced reaction were detd. The photolysis of the same system using stationary irradn. was also investigated allowing the end product of the reaction to be detd.

IT **128507-00-6P**
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in photolysis of hexachloroplatinate-creatinine methanol system)
RN 128507-00-6 CAPLUS
CN Platinate(2-), (2-amino-1,5-dihydro-1-methyl-4H-imidazol-4-one-N3)pentachloro-, (OC-6-21)- (9CI) (CA INDEX NAME)



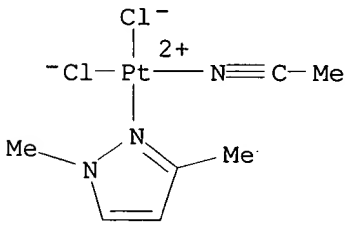
L21 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:184755 CAPLUS
DOCUMENT NUMBER: 110:184755

TITLE: Dynamic and static trans effect of acetonitrile in platinum(II) complexes
AUTHOR(S): Krol, I. A.; Kukushkin, V. Yu.; Starikova, Z. A.; Tkachuk, V. M.; Zhadanov, B. V.
CORPORATE SOURCE: USSR
SOURCE: Zhurnal Obshchei Khimii (1988), 58(11), 2625-6
CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Russian

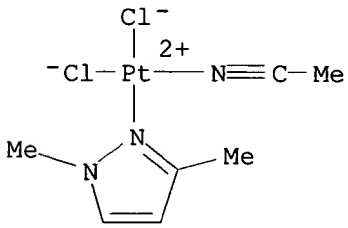
AB Et4N[Pt(MeCN)Cl3] (I) reacted with pyridine in aq. soln. to give trans-Pt(MeCN)pyCl2 (II) whereas I reacted with other amines to give cis- and trans-Pt(MeCN)LCl2 (III; L = benzimidazole, 2,5-dimethylpyrazole, PhNH2, p-anisidine). In Me2CO or MeCN trans-II is in equil. with cis-II. The formation of trans-III and the isomerization of trans-II confirm the high dynamic trans effect of MeCN in Pt(II) complexes. I is monoclinic, space group P21/c, with a 7.335(3) b 17.352(3), c 12.942(3) .ANG., .beta. 101.92(4).degree., dc = 1.984(3) g cm-3, Z = 4. The Pt-Cl bond for the Cl trans to MeCN is 2.262 .ANG. whereas the Pt-Cl bonds for cis Cl's are 2.293 and 2.301 .ANG., which indicate the high static trans effect of the Cl in comparison to MeCN. cis-Pt(MeCN)2Cl2 reacted with MCl to give M[Pt(MeCN)Cl3] (M = PPh4+, Ph3PCH2Ph+, AsPh4+, Et4N+, Bu4N+). Ph3PCH2Ph[Pt(MeCN)Cl3] was also obtained by dissoln. of (Ph3PCH2Ph)2[Pt2(.mu.-Cl)2Cl4] in MeCN or by the reaction of (Ph3PCH2Ph)2[Pt(NO2)Cl3] with Ti2(SO4)3 in MeCN-H2O.

IT **119341-13-8P**, cis-(Acetonitrile)dichloro(2,5-dimethylpyrazole)platinum **119433-34-0P**, trans-(Acetonitrile)dichloro(2,5-dimethylpyrazole)platinum
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 119341-13-8 CAPLUS
CN Platinum, (acetonitrile)dichloro(1,3-dimethyl-1H-pyrazole-N2)-, (SP-4-3)-(9CI) (CA INDEX NAME)



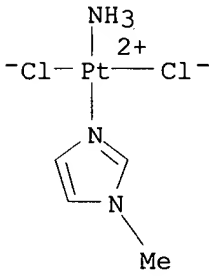
RN 119433-34-0 CAPLUS
CN Platinum, (acetonitrile)dichloro(1,3-dimethyl-1H-pyrazole-N2)-, (SP-4-1)-(9CI) (CA INDEX NAME)



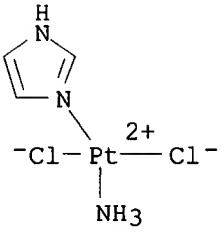
L21 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:215259 CAPLUS
DOCUMENT NUMBER: 108:215259

Searched by Barb O'Bryen, STIC 308-4291

TITLE: Synthesis and characterization of new platinum(II) complexes containing thiazole and imidazole donors
AUTHOR(S): Muir, Mariel M.; Cadiz, Mayra E.; Baez, Adriana
CORPORATE SOURCE: Dep. Chem., Univ. Puerto Rico, Rio Piedras, 00932, P. R.
SOURCE: Inorganica Chimica Acta (1988), 151(3), 209-13
CODEN: ICHAA3; ISSN: 0020-1693
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cis-Pt(NH3)LCl2 (L = thiazole, 2-bromothiazole, benzothiazole, 2,1,3-benzothiadiazole, 1,2,3-benzothiadiazole, imidazole, 1-methylimidazole) were prepd. The complexes were characterized by IR and UV-visible spectroscopy, 1H NMR and elemental analyses. The thiazoles and benzothiazoles were coordinated through the N heteroatom. Both the benzothiadiazoles were coordinated through S. Several of the complexes showed significant cytotoxic activity.
IT **114487-38-6P 114487-39-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 114487-38-6 CAPLUS
CN Platinum, amminedichloro(1-methyl-1H-imidazole-.kappa.N3)-, (SP-4-3)-(9CI) (CA INDEX NAME)



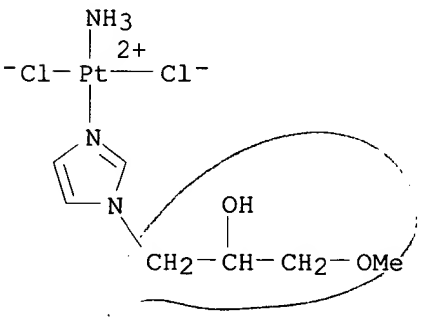
RN 114487-39-7 CAPLUS
CN Platinum, amminedichloro(1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



L21 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:529989 CAPLUS
DOCUMENT NUMBER: 107:129989
TITLE: Assessment of DNA binding of platinum-radiosensitizer complexes by inhibition of restriction enzymes
AUTHOR(S): Skov, Kirsten A.; Adomat, Hans; Konway, Desmond C.; Farrell, Nicholas P.
CORPORATE SOURCE: Med. Biophys. Unit, British Columbia Cancer Res. Cent., Vancouver, BC, V5Z 1L3, Can.
SOURCE: Chemico-Biological Interactions (1987), 62(2), 117-29
CODEN: CBINA8; ISSN: 0009-2797

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A simple and rapid method has been used to compare the binding of Pt complexes to DNA, in a relatively qual. manner. A compd. bound at or near the restriction site inhibits enzymic cleavage of DNA; inhibition of BamHI and EcoRI activities by complexes was assessed in this study using linearized pSV2-gpt plasmid. The particular interest was in DNA binding by complexes of Pt with known org. radiosensitizers (RS), to det. whether the Pt was able to target the RS to the DNA. Although the PT-RS complexes investigated themselves have moderate radiosensitizing ability (like the inorg. complexes, cis- or trans-DDP), none of the Pt-RS inhibit to the same extent as cis- or trans-DDP. However, there appears to be some correlation between enhanced radiosensitization by Pt-RS over Pt(RS)2, with the degree of Pt binding (as assessed by the assay). The results using isolated DNA suggest that not all complexes bind well (e.g., Pt with 2 RS ligands), but that in certain cases (e.g., Pt with only 1 RS), it is possible to target the drug to the DNA. An ammine or amine ligand may be required to target a radiosensitizer to DNA using Pt.
IT **110321-21-6**
RL: BIOL (Biological study)
(DNA binding of, restriction enzymes inhibition in assessment of, radiosensitization in relation to)
RN 110321-21-6 CAPLUS
CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



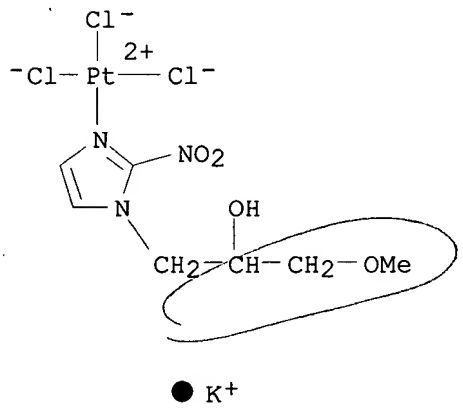
L21 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:497782 CAPLUS
DOCUMENT NUMBER: 103:97782
TITLE: Platinum(II) complexes of nitroimidazoles: synthesis, characterization, and x-ray crystal structures of cis-dichlorobis[1-(2'-hydroxyethyl)-2-hydroxymethyl-5-nitroimidazole]platinum(II) and trans-dichlorobis[1-(2'-hydroxy-3'-methoxypropyl)-2-nitroimidazole]platinum(II)
AUTHOR(S): Bales, John R.; Mazid, Muhammed A.; Sadler, Peter J.; Aggarwal, Aneel; Kuroda, Reiko; Neidle, Stephen; Gilmour, David W.; Peart, Barry J.; Ramsden, Christopher A.
CORPORATE SOURCE: Dep. Chem., Birkbeck Coll., London, WC1E 7HX, UK
SOURCE: Journal of the Chemical Society, Dalton Transactions: Inorganic Chemistry (1972-1999) (1985), (4), 795-802
CODEN: JCDTBI; ISSN: 0300-9246
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Twenty complexes PtL2X2 (I; L = substituted 5-nitroimidazole; X = Cl, Br, iodo; X2 = ethylmalonate, cyclobutane-1,1-dicarboxylate) were prepd. and characterized. I have a cis stereochem., as exemplified by the x-ray crystal-structure detn. of I [L = 1-(2'-hydroxyethyl)-2-(hydroxymethyl)-5-

nitroimidazole, X = Cl; II] using the heavy-atom method, with full-matrix least-squares refinement to R = 0.038 for 1102 obsd. reflections. Crystals of II are orthorhombic, space group Pcan, with a 8.643(1), b 24.052(3), c 9.119(1) .ANG., Z = 4, and d.(calcd.) = 2.243 g/cm3. Several analogous complexes of 2-nitro- and 4-nitroimidazoles were prepd. The geometry of the latter complexes was not detd., but the 2-nitroimidazoles form the thermodynamically favored trans complexes, rather than the kinetically favored cis complexes. This was verified by an x-ray crystal-structure detn. of trans-Pt(L1)2X2 [III; L1 = 1-(2'-hydroxy-3'-methoxypropyl)-2-nitroimidazole, X = Cl]. Crystals of III are monoclinic, space group P21/a, with a 8.134(1), b 13.014(1), c 11.323(2) .ANG., .beta. 91.469(9).degree., and d.(calcd.) = 1.85 g/cm3; the structure was refined to R = 0.054 for 1706 obsd. reflections. There is an unusual loss of planarity in III between the NO2 group and the imidazole ring, giving a dihedral angle of 45.6.degree.. Coordination of the nitroimidazole ligand to Pt(II) lowered the wavelength of the .pi.-.pi.* electronic absorption band, and reduced the polarog. redn. potential by .apprx.0.15-0.2 V.

IT **97697-89-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 97697-89-7 CAPLUS

CN Platinate(1-), trichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, potassium, (SP-4-2)- (9CI) (CA INDEX NAME)



L21 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

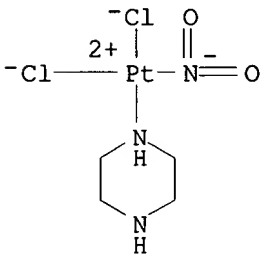
ACCESSION NUMBER: 1986:80839 CAPLUS
DOCUMENT NUMBER: 104:80839
TITLE: Synthesis and antitumor activity of platinum complexes of protonated diamines
AUTHOR(S): Doran, Sheryl L.; Khokhar, Abdul R.; Hacker, Miles P.
CORPORATE SOURCE: Tumor Inst., M. D. Anderson Hosp., Houston, TX, 77025, USA
SOURCE: Inorganica Chimica Acta (1985), 108(2), 113-15
CODEN: ICHAA3; ISSN: 0020-1693
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cis-[Pt(HQ)(L)Cl2], (Q = 3-aminoquinuclidine, N-aminopiperidine, piperazine, N-methylpiperazine, 1,1,4-trimethylpiperazine, and N-methyl-1,4-diazabicyclo[2.2.2]octane and L = SCN-, NO2-, Br-, and F-) were prepd. from [Pt(HQ)Cl3]. The antitumor activities of the complexes were evaluated in vitro against L1210 murine leukemia cells, and ID50 values for the L-substituted complexes were compared to values of the parent complexes. In each case replacement of a chloride ion by SCN-, NO2-, Br-, or F-, either reduced or completely eliminated antitumor

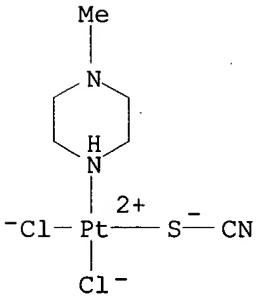
activity. This effect is explained in terms of the trans-directing ability of the ligand L, compared to chloride. The NO2-substituted complex of 3-aminoquinuclidine was tested in vivo and found to exhibit little or no antitumor activity.

IT **100226-99-1P 100227-00-7P 100227-01-8P 100227-04-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antitumor activity of, trichloro analog in relation to)

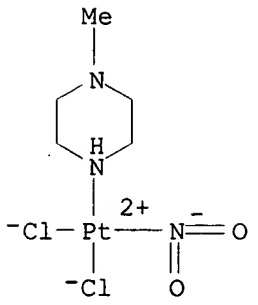
RN 100226-99-1 CAPLUS
CN Platinate(1-), dichloro(nitrito-N)(piperazine-N1)-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



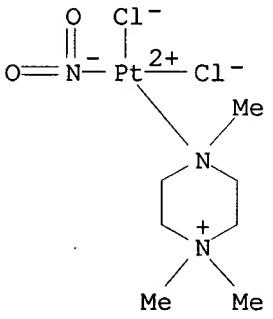
RN 100227-00-7 CAPLUS
CN Platinate(1-), dichloro(1-methylpiperazine-N4)(thiocyanato-S)-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 100227-01-8 CAPLUS
CN Platinate(1-), dichloro(1-methylpiperazine-N4)(nitrito-N)-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 100227-04-1 CAPLUS
CN Platinum, dichloro(nitrito-N)(1,1,4-trimethylpiperazinium-N4)-, (SP-4-3)-(9CI) (CA INDEX NAME)



L21 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1982:181154 CAPLUS
DOCUMENT NUMBER: 96:181154
TITLE: Anticarcinogenic organic platinum complexes
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 56158763	A2	19811207	JP 1980-61522	19800509

PRIORITY APPLN. INFO.: JP 1980-61522 19800509

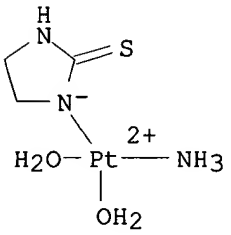
AB Stirring 0.338 g AgNO3 with 0.3 g cis-([pt(NH3)2Cl2] in H2O overnight at room temp. gave cis-[Pt(NH3)2(H2O)2](NO3)2, which was mixed with 0.111 g 2-mercaptopyridine in H2O, made pH 7 with 2 N aq. NaOH, and stirred with ice cooling to give [PtNH3(H2O)2(C5H4NS)](NO3) (I, C5H4NS = 2-mercaptopyridine residue) (yield not given). Also prepd. were Pt(NH3)(H2O)(C5H4NS)2 and (Pt(NH3)(H2O)2(C3H5N2S)](NO3) (C3H5N2S = ethylenethiourea residue). I at 100 mg/kg i.p. increased the survival time of sarcoma 180-infested mice by 244% over controls.

IT **81579-69-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antineoplastic activity of)
RN 81579-69-3 CAPLUS
CN Platinum(1+), amminediaqua(2-imidazolidinethionato-N1)-, (SP-4-3)-, nitrate (9CI) (CA INDEX NAME)

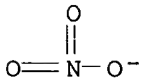
CM 1

CRN 81579-68-2
CMF C3 H12 N3 O2 Pt S
CCI CCS



CM 2

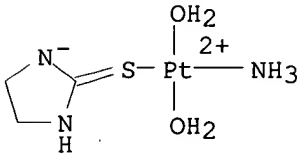
CRN 14797-55-8
CMF N O3



L21 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:166780 CAPLUS
DOCUMENT NUMBER: 94:166780
TITLE: Synthesis and antitumor activity of platinum complexes with cyclic thioamides
AUTHOR(S): Fujieda, Sigeaki; Tabata, Esuzu; Hatano, Akiko; Osa, Tetsuo
CORPORATE SOURCE: Pharm. Inst., Tohoku Univ., Sendai, 980, Japan
SOURCE: Heterocycles (1981), 15(2), 743-6
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complexes [Pt(NH3)(H2O)2L]NO3 and [Pt(NH3)(H2O)L2] (HL = 2-mercaptopyridine (I), 2-thiouracil (II), ethylenethiourea (III)) were prepd. and their activity against Sarcoma 180 in mice was tested. Both complexes of I showed high antitumor activity but only the complex contg. 1 ligand of III was effective. The complexes of II had little antitumor activity.
IT **77319-89-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and antitumor activity of)
RN 77319-89-2 CAPLUS
CN Platinum(1+), amminediaqua(2-imidazolidinethionato-S)-, (SP-4-2)-, nitrate (9CI) (CA INDEX NAME)

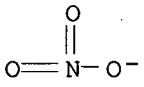
CM 1

CRN 77319-88-1
CMF C3 H12 N3 O2 Pt S
CCI CCS



CM 2

CRN 14797-55-8
CMF N O3



L21 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:145351 CAPLUS
DOCUMENT NUMBER: 88:145351
TITLE: New piperazinium complex salts with antitumour action
AUTHOR(S): Doadrio, A.; Craciunescu, D.; Ghirvu, G.
CORPORATE SOURCE: Dep. Inorg. Anal. Chem., Fac. Pharm., Madrid, Spain
SOURCE: Anales de Quimica (1968-1979) (1977), 73(7-8), 1042-6
CODEN: ANQUBU; ISSN: 0365-4990
DOCUMENT TYPE: Journal
LANGUAGE: English

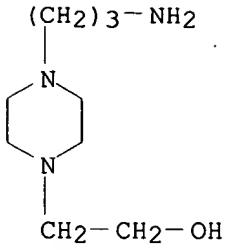
AB The salts [LH2][PtCl6], [LH2][OsCl6], and [LH2][CuCl4], where L = piperazine and its derivs. such as 1-methylpiperazine, 1-piperazineethanol, 1,4-bis(2-hydroxyethyl)piperazine, 4-(3-aminopropyl)-1-piperazineethanol, were prepd. and characterized by IR, magnetic, and conductimetric data, and their antitumor activities are reported. The electronic charge is localized to a much greater extent on the ring N atoms than on any exocyclic amino group.

IT **65703-85-7P 66098-32-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., electronic charge localization and antitumor activity of)

RN 65703-85-7 CAPLUS
CN Platinate(2-), hexachloro-, (OC-6-11)-, dihydrogen, compd. with 4-(3-aminopropyl)-1-piperazineethanol (1:1) (9CI) (CA INDEX NAME)

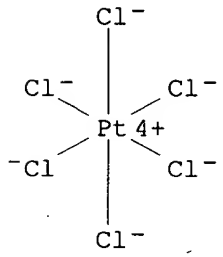
CM 1

CRN 58110-73-9
CMF C9 H21 N3 O



CM 2

CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS

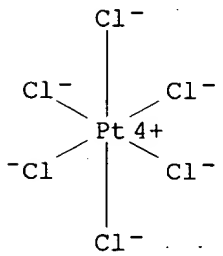


2 H^+

RN 66098-32-6 CAPLUS
CN Platinate(2-), hexachloro-, (OC-6-11)-, dihydrogen, compd. with 1-piperazineethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

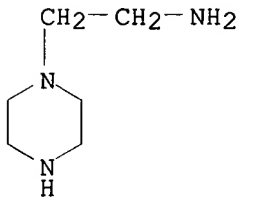
CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS



2 H^+

CM 2

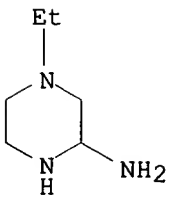
CRN 140-31-8
CMF C6 H15 N3



L21 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:499758 CAPLUS
DOCUMENT NUMBER: 89:99758
TITLE: Effects of the compounds (PtCl6)H2(3-piperazinyl-1-ethylamine) and (OsCl6)H2(aminopyrine)2 on calcium and sodium transport in isolated frog skin
AUTHOR(S): Anadon, A.; Craciunescu, D.; Doadrio, A.; Larranaga, M. R. M.; Sanz, F.
CORPORATE SOURCE: Fac. Vet., Univ. Madrid, Madrid, Spain
SOURCE: Acta Pharmaceutica Fennica (1977), 86(4), 203-7
CODEN: APHFDO; ISSN: 0356-3456
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study was conducted on the effects of the salt complexes (PtCl6)H2(3-piperazinyl-1-ethylamine) [**66632-41-5**] and (OsCl6)H2(aminopyrine)2 [65230-73-1] on elec. potentials, Na transport and Ca diffusion in frog skin used as a model membrane in an attempt to understand their pharmacol. effects. The results indicate that the salt complex (OsCl6)H2(aminopyrine)2 decreases both the transport of Na and elec. potential, and inhibits the effect of CaCl2. The salt complex (PtCl6)H2(3-piperazinyl-1-ethylamine) does not exhibit any effect.
IT **66632-41-5**
RL: BIOL (Biological study)
(calcium and sodium transport by cell membrane response to)
RN 66632-41-5 CAPLUS
CN Platinate(2-), hexachloro-, (OC-6-11)-, dihydrogen, compd. with 4-ethyl-2-piperazinamine (1:1) (9CI) (CA INDEX NAME)

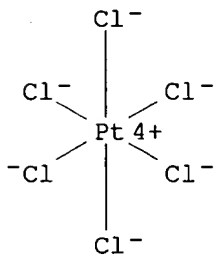
CM 1

CRN 66632-40-4
CMF C6 H15 N3



CM 2

CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS

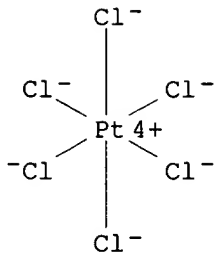


2 H^+

L21 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1966:44120 CAPLUS
DOCUMENT NUMBER: 64:44120
ORIGINAL REFERENCE NO.: 64:8277b-c
TITLE: Aminolysis of sucrose. VI. Reaction between sucrose and aqueous .beta.-aminopropionitrile solution at increased temperatures
AUTHOR(S): Jezo, I.; Luzak, I.
CORPORATE SOURCE: Slovenska Akad. Vied, Bratislava, Czech.
SOURCE: Chemicke Zvesti (1965), 19(12), 900-7
CODEN: CHZVAN; ISSN: 0366-6352
DOCUMENT TYPE: Journal
LANGUAGE: Czech
AB cf. CA 63, 665f. Reaction of sucrose with aq. .beta.-aminopropionitrile soln. at higher temps. gave a mixt. of compds.: 2-methylpyrazine (b751 132-4.degree., n20D 1.5056; picrate m. 132-3.degree.) 2,5-dimethylpyrazine (b751 152-4.degree., n20D 1.5040; picrate 155-6.degree.), 2-methyl-1,4(?)-dihydropyrazine (b10 45-8.degree., n20D 1.5000, d20 1.0042; picrate m. 172.degree.), 4(5)-methylimidazole, and 2-methyl-4-(.beta.-cyanoethyl)-1,4-dihydropyrazine, b0.01 103-5.degree., n20D 1.5016. At the same time with the formation of these compds. there is a dismutation of .beta.-aminopropionitrile with the formation of bis(2-cyanoethyl)-amine. The reaction mechanism is given.
IT **7415-10-3**, 1-Piperazinepropionitrile, 2-methyl-, hexachloroplatinate(IV)
(prepn. of)
RN 7415-10-3 CAPLUS
CN 1-Piperazinepropionitrile, 2-methyl-, hexachloroplatinate(IV) (7CI, 8CI) (CA INDEX NAME)

CM 1

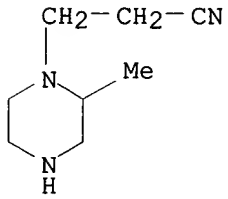
CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS



2 H^+

CM 2

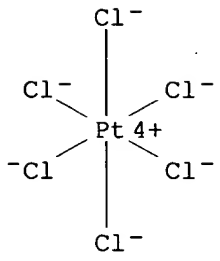
CRN 6216-09-7
CMF C8 H15 N3



L21 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1965:29873 CAPLUS
DOCUMENT NUMBER: 62:29873
ORIGINAL REFERENCE NO.: 62:5322f-g
TITLE: Aminolysis of sucrose. IV. Reaction of sucrose with aqueous solution of ethylenediamine
AUTHOR(S): Jezo, Ivan; Luzak, Ivan
CORPORATE SOURCE: Slovak Acad. Sci., Bratislava, Czech.
SOURCE: Chemicke Zvesti (1964), 18(3), 186-98
CODEN: CHZVAN; ISSN: 0366-6352
DOCUMENT TYPE: Journal
LANGUAGE: Slovak
AB cf. CA 61, 2039a. The aminolysis of sucrose was carried out with an aq. soln. of ethylenediamine. The following compds. were isolated and identified: 2-methyl-2-imidazoline, 2-ethyl-2-imidazoline, 2-hydroxy-6,7-dihydro-8-azaquinolizine, piperazino[a]-3-hydroxy-8-azaquinolizidine and piperazino[a]-3-hydroxy 8-aza-.DELTA.8,9(9,10)-dehydroquinolizidine. A reaction mechanism is proposed.
IT **2870-74-8**, 2-Piperazineacetonitrile, hexachloroplatinate(IV) (prepn. of)
RN 2870-74-8 CAPLUS
CN 2-Piperazineacetonitrile, hexachloroplatinate (8CI) (CA INDEX NAME)

CM 1

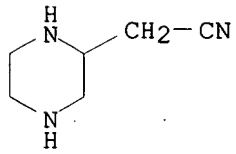
CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS



2 H^+

CM 2

CRN 2465-79-4
CMF C6 H11 N3



L21 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1962:469229 CAPLUS
DOCUMENT NUMBER: 57:69229
ORIGINAL REFERENCE NO.: 57:13756a-h
TITLE: Synthesis of potential anticancer agents. XXX. (1-Aziridinyl)purines
AUTHOR(S): Montgomery, J. A.; Hewson, K.; Temple, C.,Jr.
CORPORATE SOURCE: Southern Res. Inst., Birmingham, AL
SOURCE: Journal of Medicinal & Pharmaceutical Chemistry (1962), 5, 15-24
CODEN: JMPCAS; ISSN: 0095-9065
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 57:69229

AB cf. CA 56, 1445a. Eight (1-aziridinyl) purines were prepd. by nucleophilic displacement of the Cl in the corresponding chloropurines. The compds. were screened against Ca 755 and Walker 256, and the 6-(1-aziridinyl)purines show moderate activity against the Ca 755, and in 1 case good activity against Walker 256. 6-(1-Aziridinyl)-9-benzyl-9H-purine (I) (100 mg.) in 10 ml. EtOH was hydrogenated at room temp./atm. pressure with 50 mg. 5% Pd-C catalyst 18 hrs., the catalyst filtered off, the filtrate evapd. to dryness, the residue dissolved in 10 ml. 0.1N HCl, the soln. evapd. to dryness in vacuo, the residue triturated with 10 ml. Me2CO, the ppt. filtered off, and dried in vacuo to give 90 mg. 9-benzyl-N6-ethyl-adenine-HCl. I can also be reduced with metallic Na in liquid NH3 to give N6-ethyladenine, m. 227-8.degree. (decompn.). A mixt. of 5.7 g. 2,6-dichloropurine, 6.9 ml. benzyl chloride, 4.2 g. K2CO3, and 50 ml. Me2SO was stirred 18 hrs., filtered, the filtrate concd. to one-quarter vol. in vacuo, poured into ice-H2O, the oil allowed to solidify, filtered, washed with H2O, air dried, and recrystd. from 75% aq.

EtOH with Norit treatment to give 5.9 g. of a mixt. of the 7- and 9-isomers of benzyl-2,6-dichloro-9H-purine, m. 122-30.degree.. Recrystn. from MeOH gave 1.06 g. pure 9-isomer, m. 148.degree.. The mother liquors from the recrystn. gave 30% yield of the 7-isomer. contaminated with the 9-isomer. Prepd. similarly was 2-amino-9-benzyl-6-chloro-9H-purine, and 2-amino-7-benzyl-6-chloro-7H-purine. 9-Benzyl-2,6-di-chloropurine (278 mg.) in 10 ml. 0.2N naOH was refluxed with stirring to effect soln., the hot mixt. filtered, the filtrate acidified with glacial HOAc, the ppt. filtered off, washed with dil. HOAc, and dried in vacuo to give 233 mg. 9-benzyl-2-chlorohypoxanthine (II), m. 245.degree.. II (100 mg.) in 15 ml. abs. EtOH was placed in a glass-lined Parr bomb, satd. with dry NH3 at 5.degree., the soln. heated 6 hrs. at 150.degree., the bomb chilled, opened, the soln. concd. to 10 ml. in a stream of dry n, the solid filtered off, washed with EtOH, and dried in vacuo to give 53 mg. 9-benzylguanine (III), m. 303.degree.. III may also be prepd. from 2-amino-9-benzyl-6-chloropurine by reaction with HCl. II (0.29 millimole) and 0.2 ml. 25% aq. dimethylamine were dissolved in 10 ml. dioxane, the mixt. heated 20 hrs. at 95-100.degree., with an addn. of another quantity of Me2NH at the end of the first 2 hrs., the mixt. evapd. to dryness in vacuo, the residue triturated with Et2O, and the residue recrystd. from EtOH to give 57 mg. 9-benzylN2,N2-dimethylguanine, m. 282.degree.. 7-Benzyl-2,6-dichloropurine (contaminated with the 9-isomer) (1.11 g.) in 25 ml. n NaOH was heated 1.5 hrs. at 115.degree., cooled to room temp., kept overnight in the refrigerator, the solid filtered off, dissolved in H2O, acidified with glacial HOAc, the solid filtered off, dried in vacuo, and recrystd. from abs. EtOH to give 60 mg. 7-benzyl-2-chlorohypoxanthine, m. 285.degree. 6,8-Dichloropurine (1.06 g.), 0.69 g. anhyd. K2CO3, and 1.4 ml. PhCH2Cl in 10 ml. HCONMe2 was heated 1 hr. at 70-85.degree. with stirring, concd. to 0.5 vol. in vacuo, poured into ice-H2O, the oil extd. with Et2O, the ext. dild. with EtOH, the solid filtered off, washed with Et2O, dried, extd. with Skellysolve C, the ext. evapd. to an oil, dissolved in 1:1 aq. EtOH, the solid filtered off, washed with H2O, dried in vacuo over P2O5 at room temp., and recrystd. from aq. EtOH to give 203 mg. 9-benzyl-6,8-dichoro-9H-purine, m. 92.degree.. Prepd. by similar methods was 9-benzyl-6-dimethylamino-9H-purine, m. 117.degree.. 9-Benzyl-6-dimethylamino-8-chloropurine (307 mg.), 43 mg. MgO, and 34 mg. 5% Pd-C in 30 ml. abs. EtOH was hydrogenated at atm. pressure 6 hrs., the catalyst filtered off, the filtrate evapd. to dryness, and the residue triturated with EtOH to give 135 mg. 9-benzyl-6-dimethylaminopurine, m. 128.degree..

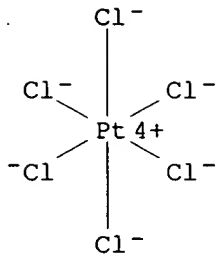
IT **94071-79-1**, Piperazine, 1-(2-aminoethyl)-4-ethyl-, hexachloroplatinate(IV)
(prepn. of)

RN 94071-79-1 CAPLUS

CN Piperazine, 1-(2-aminoethyl)-4-ethyl-, hexachloroplatinate(IV) (7CI) (CA INDEX NAME)

CM 1

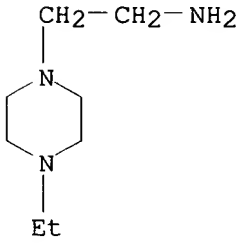
CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS



2 H^+

CM 2

CRN 4489-46-7
CMF C8 H19 N3



L21 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1962:469228 CAPLUS
DOCUMENT NUMBER: 57:69228
ORIGINAL REFERENCE NO.: 57:13755f-i,13756a
TITLE: Condensation reaction of amino alcohols with imides. IV. Condensation products of .beta.-(cycloamino)ethanols with succinimide and with phthalimide-formation of .beta.-(cycloamino)ethylamines
AUTHOR(S): Nakajima, Kazuo
CORPORATE SOURCE: Teikoku Chem. Ind., Mibukayogosho, Kyoto
SOURCE: Nippon Kagaku Zasshi (1960), 81, 1129-32
CODEN: NPKZAZ; ISSN: 0369-5387
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. CA 57, 8545h. Seven aminoalcs. (RNCH2CH2OH) (I), where RN = (CH2)4N (a), (CH2)5N (b), .beta.-tetrahydroquinoline (c), morpholino (d), 4-ethylpiperazino (e), 4-butylpiperazino (f), and 4-phenylpiperazino (g). I and phthalimide heated at 200.degree. while removing the H2O formed yielded RNCH2CH2N(CO)2C6H4-o (II) (RN, m.p., b10, m.p. of picrate, and decompn. point of Pt salt given): a, 109.degree., 220.degree., 218.degree., 212.degree.; b, 90.degree., 206.degree., 215.degree., 215.degree.; c, 137.degree., 273.degree., 144.degree., 204.degree.; d, 135.degree., 216.degree., 232.degree., 146.degree.; e, 115.degree., 227.degree., 245.degree. (decompn.), 265.degree.; f, 75.degree., 252.degree., 260.degree. (decompn.), 271.degree.; g, 158.degree., 279.degree., 218.degree. (decompn.), 262.degree.. Similarly, I and

succinimide yielded RNCH2CH2N(COCH2)2 (III) (RN, m.p., b10, m.p. of picrate, and decompn. point of Pt salt given): a, 55.degree., 170.degree., 158.degree., 212.degree.; b, -, 170.degree., 190.degree., 230.degree.; c, 115.degree., 210.degree., 180.degree., -; d, 75.degree., 170.degree., 181.degree., 175.degree.; e, -, 199.degree., 245.degree., 245.degree.; f, 65.degree., 223.degree., 225.degree., 255.degree.; g, 141.degree., 272.degree., 175.degree., 236.degree.. II and III refluxed with 20% HCl 3-5 hrs., phthalic acid or succinic acid filtered off, and the filtrate concd. yielded RNCH2CH2NH2.HCl (IV.HCl). Free RNCH2CH2NH2 (IV) was obtained by a long extn. of neutralized IV.HCl with ether. (RN, b10, b760, m.p. of picrate, and decompn. point of Pt salt given) a, 33.degree., 165-6.degree., 210.degree. (decompn.), 207.degree.; b, 50.degree., 185.degree., .apprx.200 (decompn.), 218.degree.; c, 157.degree., 290.degree., -, -; d, 81.degree., 204.degree., 177.degree. (decompn.), 237.degree.; e, 88.degree., 223-4.degree., 230.degree., 270.degree.; f, 120.degree., 255.degree., 116.degree., 252.degree.; g, (m. 80.degree.), 191.degree., 326.degree., -. 210-40.degree..

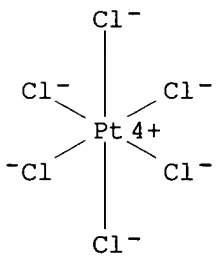
IT **94071-79-1**, Piperazine, 1-(2-aminoethyl)-4-ethyl-, hexachloroplatinate(IV) **94387-55-0**, Piperazine, 1-(2-aminoethyl)-4-butyl-, hexachloroplatinate(IV)
(prepn. of)

RN 94071-79-1 CAPLUS

CN Piperazine, 1-(2-aminoethyl)-4-ethyl-, hexachloroplatinate(IV) (7CI) (CA INDEX NAME)

CM 1

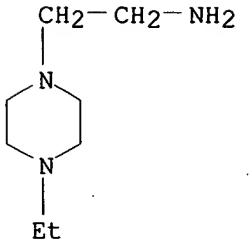
CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS



2 H^+

CM 2

CRN 4489-46-7
CMF C8 H19 N3



RN 94387-55-0 CAPLUS
CN Piperazine, 1-(2-aminoethyl)-4-butyl-, hexachloroplatinate(IV) (7CI) (CA INDEX NAME)

CM 1

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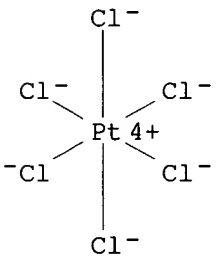
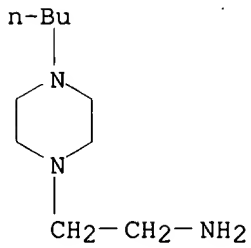
CMF Cl6 Pt . 2 H
CCI CCS



2 H^+

CM 2

CRN 4489-55-8
CMF C10 H23 N3



L21 ANSWER 26 OF 26 USPATFULL on STN
ACCESSION NUMBER: 2003:40793 USPATFULL
TITLE: Process for preparing amine platinum complexes
INVENTOR(S): Wong, Ernest S. Y., Langley, CANADA
Gianomenico, Christen M., Blaine, WA, United States

PATENT ASSIGNEE(S): Anormed, Inc., Langley B.C., CANADA (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6518428	B1	20030211
APPLICATION INFO.:	US 2000-547074		20000411 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-128939P	19990413 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Huang, Evelyn Mei
LEGAL REPRESENTATIVE: Morrison & Foerster LLP
NUMBER OF CLAIMS: 33
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1148
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the area of platinum drugs. In particular, it relates to an improved process for preparing platinum complexes having the general formula (Ia) or (Ib): as defined of herein, ##STR1##

comprising:

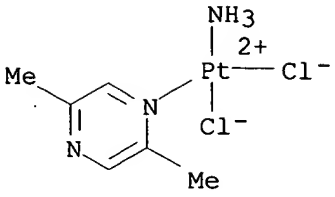
1a) a first step, wherein [PtA.sub.4].sup.2- is reacted with L under appropriate conditions in a first solvent to form [PtA.sub.3(L)].sup.-;

1b) a second step, wherein [PtA.sub.3(L)].sup.- is reacted with L' under appropriate conditions in a second solvent to form cis-[PtA.sub.2(L')(L)];

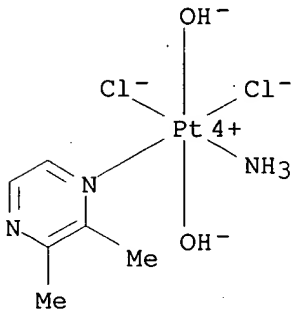
1c) in the case where Y is halogen or hydroxy a third step, wherein cis-[PtA.sub.2(L')(L)] is reacted with H.sub.2O.sub.2, Y.sub.2 or halogen containing oxidant to form c,t,c-[PtA.sub.2Y.sub.2(L')(L)]; in the case where Y is carboxylate, carbamate or carbonate ester a fourth step, wherein an intermediate, where Y is hydroxy formed in step 1c), is functionalized with an appropriate acylating agent; and

1d) in the case where A is not a halide or is different from the original halide, additional step(s) in which the original halide A of an intermediate formed in step 1a or 1b 1c or 1d is converted to a different halide or a new leaving group(s) A such as mono-dentate hydroxy, alkoxy, carboxylate or bi-dentate carboxylate, phosphonocarboxylate, diphosphonate, or sulphate.

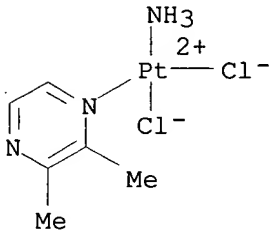
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **301299-27-4P 301299-34-3P**
(improved prepn. of antitumor agent)
RN 301299-27-4 USPATFULL
CN Platinum, amminedichloro(2,5-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 301299-34-3 USPATFULL
CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)dihydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)



IT **301299-38-7**
(reactant for improved prepn. of platinum amine complexes as antitumor agents)
RN 301299-38-7 USPATFULL
CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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                L13)) OR (2/N AND L10))
L16          52 SEA FILE=REGISTRY ABB=ON  L15 AND 1/NR
L20           4 SEA FILE=CAOLD ABB=ON  L16


=> d iall hitstr l20 1-4

L20  ANSWER 1 OF 4  CAOLD  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:  CA64:8277b  CAOLD
TITLE:             aminolysis of sucrose - (VI) reaction between sucrose and
                   aq. .beta.-aminopropionitrile soln. at increased temps.,
                   (VII) reaction between sucrose and an aq. soln. of
                   dimethylamine at higher temps.
AUTHOR NAME:       Jezo, Ivan; Luzak, I.
INDEX TERM:         151-18-8   6216-07-5   6216-08-6   6216-09-7   6216-10-0
                   6216-15-5   6372-03-8   7365-19-7   7415-09-0
                   7415-10-3   7437-30-1  91144-97-7
IT   7415-10-3
RN   7415-10-3  CAOLD
CN   1-Piperazinepropionitrile, 2-methyl-, hexachloroplatinate(IV) (7CI, 8CI)
     (CA INDEX NAME)

     CM   1

     CRN  16941-12-1
     CMF  C16 Pt . 2 H
     CCI  CCS
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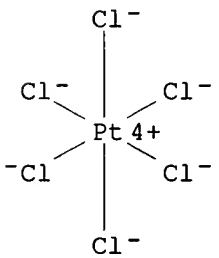
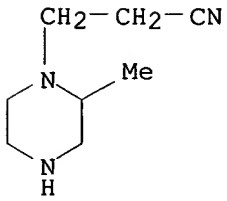


2 H^+

CM 2

CRN 6216-09-7
CMF C8 H15 N3



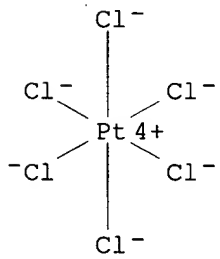
L20 ANSWER 2 OF 4 CAOLD COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: CA62:5322g CAOLD
TITLE: prepn. and use of .beta.-cyanoethylated polyhydric alcs. in gas chromatography
AUTHOR NAME: Ratusky, Josef; Bastar, L.
INDEX TERM:

89-71-4	93-58-3	93-60-7	98-27-1	99-36-5
99-75-2	99-76-3	100-23-2	119-36-8	534-26-9
611-20-1	612-24-8	617-37-8	619-24-9	626-86-8
767-00-0	873-62-1	1070-34-4	1070-62-8	1071-46-1
1129-89-1	1459-93-4	1486-75-5	2305-59-1	2409-55-4
2459-05-4	2459-07-6	2459-09-8	2459-10-1	2459-24-7
2459-25-8	2465-78-3	2465-79-4	2465-80-7	2465-81-8
2465-82-9	2465-85-2	2465-86-3	2465-87-4	2465-88-5
2465-89-6	2465-91-0	2465-92-1	2465-93-2	2465-94-3
2484-57-3	2484-58-4	2484-59-5	2484-60-8	2484-61-9
2484-62-0	2484-64-2	2484-65-3	2484-66-4	2484-74-4
2671-74-1	2672-57-3	2672-58-4	2778-62-3	2779-94-4
2870-74-8	3990-03-2	19438-10-9	90418-99-8	
94033-42-8	94409-05-9	94409-06-0		

IT **2870-74-8**
RN 2870-74-8 CAOLD
CN 2-Piperazineacetonitrile, hexachloroplatinate (8CI) (CA INDEX NAME)

CM 1

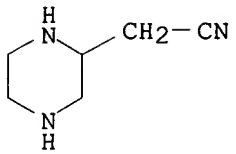
CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS



●2 H^+

CM 2

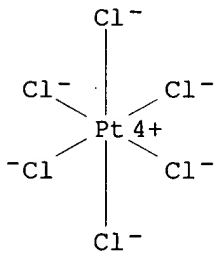
CRN 2465-79-4
CMF C6 H11 N3



L20 ANSWER 3 OF 4 CAOLD COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: CA57:13756a CAOLD
TITLE: synthesis of potential anticancer agents - (XXX) (1-aziridinyl) purines
AUTHOR NAME: Montgomery, John A.; Hewson, K.; Temple, C., Jr.
INDEX TERM: 4489-46-7 4489-55-8 6311-27-9 6332-42-9 6336-42-1
7461-80-5 14937-72-5 21091-61-2 53665-01-3 56025-87-7
56025-88-8 79064-26-9 90559-83-4 91395-18-5 92193-48-1
92291-23-1 92291-24-2 92495-26-6 93256-54-3
94071-79-1 **94387-55-0** 95194-86-8
96952-06-6 97619-37-9
IT **94071-79-1** **94387-55-0**
RN 94071-79-1 CAOLD
CN Piperazine, 1-(2-aminoethyl)-4-ethyl-, hexachloroplatinate(IV) (7CI) (CA INDEX NAME)

CM 1

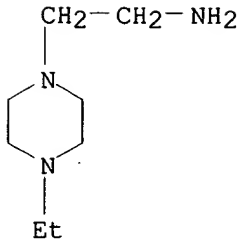
CRN 16941-12-1
CMF Cl6 Pt . 2 H
CCI CCS



2 H^+

CM 2

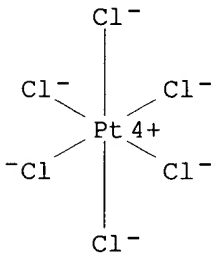
CRN 4489-46-7
CMF C8 H19 N3

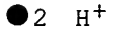


RN 94387-55-0 CAOLD
CN Piperazine, 1-(2-aminoethyl)-4-butyl-, hexachloroplatinate(IV) (7CI) (CA INDEX NAME)

CM 1

CRN 16941-12-1
CMF C16 Pt . 2 H
CCI CCS





CM 2

CRN 4489-55-8
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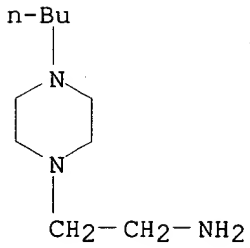

L20 ANSWER 4 OF 4 CAOLD COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: CA51:16490f CAOLD
TITLE: triethylenediamine (1,4-diazabicyclo-[2,2,2]octane) and hexaethylenetetramine - (III) interaction of 2,2',2'',-trichlorotriethylamine-HCL and dimethylamine

AUTHOR NAME: Mann, Frederick G.; Baker, F. C.
INDEX TERM: 104-19-8 283-74-9 3644-18-6 5450-74-8 6952-20-1
7699-64-1 14870-72-5 14968-74-2 14968-80-0 19479-83-5
22746-07-2 24996-75-6 36220-12-9 41809-88-5 60013-06-1
60420-20-4 65420-17-9 77267-14-2 96819-72-6 98545-14-3
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101787-23-9 101882-89-7 101882-90-0 103033-84-7 103163-44-6
103327-67-9 103401-77-0 103402-09-1 103510-04-9 107773-52-4
108129-20-0 108131-10-8 109407-12-7 109499-70-9 110055-62-4
110357-87-4 112224-31-4 112745-27-4 112745-30-9 114063-46-6
114225-70-6 114791-37-6 114985-11-4 114985-13-6 114985-51-2
115307-78-3 116032-45-2 116597-68-3 116928-68-8 117891-78-8
122238-94-2 122337-98-8 122679-89-4 123935-46-6
132984-24-8 133133-15-0

IT **122238-94-2**
RN 122238-94-2 CAOLD
CN Bis[4-(2-dimethylaminoethyl)-1,1-dimethylpiperazinium] chloroplatinate(IV) (6CI) (CA INDEX NAME)

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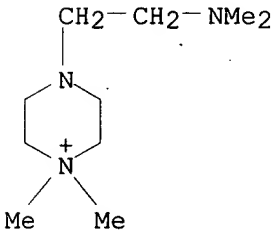
CRN 122238-93-1
CMF C10 H24 N3



CM 2

CRN 16871-54-8
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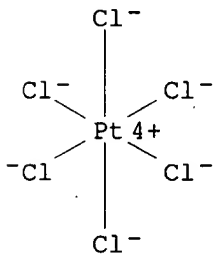

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2,3:4,5-di-*O*-isopropylidene-6-*O*-trityl-D-galactose, $[\alpha]_D^{25}$ −26.6° (*c* 1.5, $CHCl_3$), was prepd. I was isolated on preparative chromatography in $CHCl_3$ on a thin layer of Al_2O_3 as a sirup with R_f 0.64 and $[\alpha]_D^{25}$ −53.2° (*c* 1, $CHCl_3$). Jan Micka

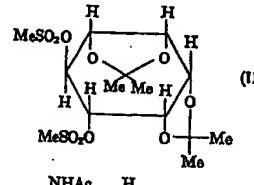
Sucrose esters. I. Chemical properties and EHL. J. Peris and J. M. Sune (Fac. Farm., Granada, Spain). *Galenica Acta* (Madrid) 17(3–4), 227–38(1964)(Span). Com. sucrose 6 and (or) 6′ mono- and di-esters with fatty acids were tested for acid index, sapon. index, and acid index of hydrolyzed fatty acids, noting purity and EHL [= 20(1 no. 14 sapon. index/acid index of esterifying acid)]. Free acidity of the esters was relatively low, and EHL values fell between those of sorbitan esters (Spans) and poly(oxyethylene) derivs. (Tweens). 45 references. Keith S. Brown

Aminolysis of sucrose. VI. Reaction between sucrose and aqueous β-aminopropionitrile solution at increased temperatures. I. Jezo and I. Luzak (Slovenska Akad. Vied, Bratislava, Czech.). *Chem. Zvesti* 19(12), 900–7(1965)(Czech); cf. *CA* 63, 665*f*. Reaction of sucrose with aq. β-aminopropionitrile soln. at higher temps. gave a mixt. of compds.: 2-methylpyrazine (b_{751} 132–4°, n_D^{20} 1.5056; picrate m. 132–3°) 2,5-dimethylpyrazine (b_{751} 152–4°, n_D^{20} 1.5040; picrate 155–6°), 2-methyl-1,4(?)-dihydropyrazine (b_{10} 45–8°, n_D^{20} 1.5000, d_{20} 1.0042; picrate m. 172°), 4(5)-methylimidazole, and 2-methyl-4-(β-cyanoethyl)-1,4-dihydropyrazine, $b_{0.01}$ 103–5°, n_D^{20} 1.5016. At the same time with the formation of these compds. there is a dismutation of β-aminopropionitrile with the formation of bis(2-cyanoethyl)-amine. The reaction mechanism is given. Jan Micka

Aminolysis of sucrose. VII. Reaction between sucrose and an aqueous solution of dimethylamine at higher temperatures. I. Jezo and I. Luzak (Slovenska Akad. Vied, Bratislava, Czech.). *Chem. Zvesti* 19(12), 908–17(1965)(Czech); cf. preceding abstr. From the mixt., formed by the reaction of sucrose with an aq. soln. of Me_2NH at higher temps., the following compds. were isolated and identified: Me_3N, Me_2NEt, 2-dimethylaminoethanol, 1,2-bis(dimethylamino)propane, 1,1,2-tris(dimethylamino)ethane, $AcNMe_2$ *N*,*N*-dimethylglycolamide, *N*,*N*,*N*′,*N*′-tetramethylglycinamide, and bis(dimethylamide) of *cis*(?)-tetrahydrofuran-2,5-dicarboxylic acid. A reaction mechanism is given. Jan Micka

Polysaccharides from Plantago major leaves. I. Analysis of monosaccharide composition of polysaccharide complex. A. G. Gorin (Chem.-Pharm. Inst. Kharkov). *Khim. Prirodn. Soedin., Akad. Nauk Uz. SSR* 1965(5), 297–302(Russ). A polysaccharide of the pectin type was isolated from the title material. Dry leaves were extd. with boiling 80% EtOH and Me_2CO, and air-dried. The polysaccharide was extd. with boiling H_2O (1:15) for 2 hrs. and pptd. with 3 vols. of EtOH (yield 10%, ash 28%). The crude prepn. (10 g.) was dissolved in H_2O (100 cc.) and percolated through a cation-exchange resin KU-2 (H^+) column (20 × 180 mm.). The demineralized soln. was poured in 4 vols. of EtOH and the pptd. polysaccharide dried by solvent exchange, yielding 4.5 g. of a prepn. $[\alpha]_D$ +195.0° (*c* 0.43, 0.3*N* NaOH), galacturonic acid content by decarboxylation 68%, equiv. wt. 454, equiv. wt. after sapon. 263, methoxyl content 4.2%. A part of the polysaccharide was hydrolyzed with 1.0*N* H_2SO_4 for 8 hrs.; D-galacturonic acid, D-galactose, L-arabinose, and L-rhamnose were characterized as cryst. derivs. Small amts. of glucose, xylose, and 3 unknown compds., one of them being identified as a di-*O*-methylgalactose, were also found. V. Zitko

Aminocyclitols. IX. The facile synthesis of streptamine. Tetsuo Suami and Seiichiro Ogawa (Keio Univ., Tokyo). *Bull. Chem. Soc. Japan* 38(11), 2026(1965)(Eng); cf. *CA* 63, 8464*f*. Streptamine was prepd. via a new route. (±)-1,2:3,4-Di-*O*-isopropylidene-*epi*-inositol (I) (Angyal and Gilham, *CA* 52, 11759*g*) was converted to II, m. 147.5–8.5°, by treatment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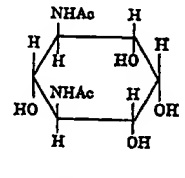
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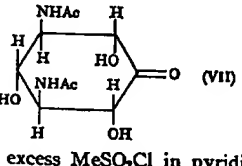
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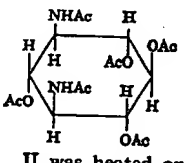
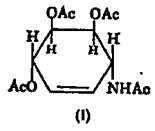

(VIII)

with excess $MeSO_2Cl$ in pyridine. II was heated on a water bath 2 hrs. in 50% HOAc and the product acetylated to give (±)-5,6-di-*O*-mesyl-*epi*-inositol tetracetate (III), m. 166.5–8.5°. Treatment of III with NaN_3 in boiling aq. 2-methoxyethanol for 40 hrs. and subsequent acetylation afforded 28% 4,6-diazido-4,6-dideoxy-*myo*-inositol tetraacetate (IV), m. 147–9°. Catalytic hydrogenation of IV in EtOH and acetylation of the product gave hexaacetyl-4,6-*myo*-inosadiamine (V), m. 290–2°. V was selectively deacetylated to VI which was oxidized with Pt black in a stream of *O* for 24 hrs. at 40° to give VII. VII was immediately reduced with Na/Hg in a slightly acidic soln. and the redn. product acetylated to give 12.5% hexaacetylstreptamine (VIII), transition point 243–8°. O. L. Marrs

Chemistry of 3,5-cyclohexadiene-1,2-diol. XIII. Synthesis of deoxyinosadiamines. Minoru Nakajima, Akira Hasegawa, and Takashi Kurokawa (Univ. Kyoto, Japan). *Ann. Chem.* 689, 229–34(1965)(Ger); cf. *CA* 62, 14796*h*. From 4 stereoisomeric *N*-acetyl-tri-*O*-acetylkonduramines (acetyl derivs. of trihydroxyaminocyclohexene) (*CA* 58, 9216*g*) were prepd. acetamido-tri-*O*-acetylinosamines by catalytic debromination of the resp. bromohydrins. These on oxidn. gave 4 stereoisomeric deoxyinosaminoses, 3 of which were converted into deoxyinosadiamines via their oximes. The assigned configurations were detd. on the basis of N.M.R. spectra. To 4 g. *N*-acetyl-tri-*O*-acetylkonduramine A 1 (I) (m. 157°) in 70 cc. H_2O and 70 cc. AcOH was added dropwise 70 cc. 3% H_2O–Br with ice cooling and the soln. let stand 2 hrs. at room temp. to give 3.6 g. II, m. 114–15°. Acetylation of II with Ac_2O–C_5H_5N gave 90%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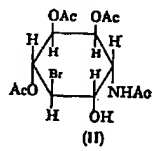
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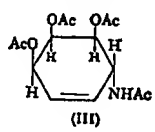
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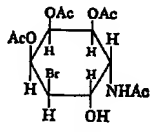
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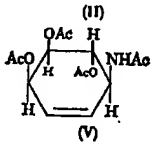
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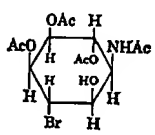
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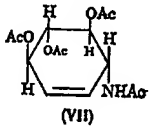
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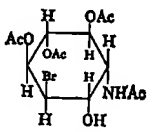
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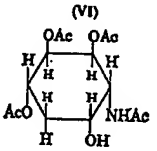
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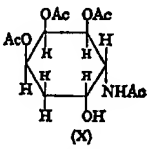
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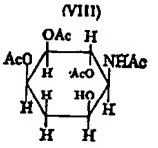
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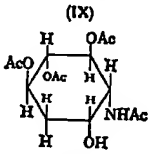
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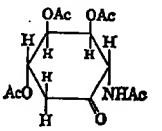
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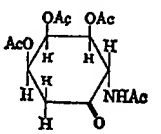
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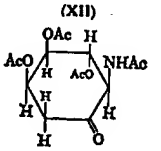
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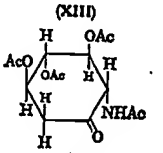
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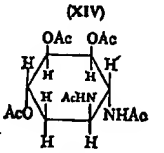
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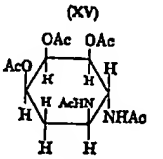
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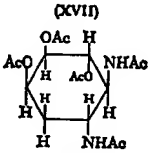

(XIX)

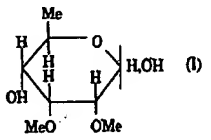
pentaacetyl deriv., m. 212–13°, identical (mixed m.p. and ir spectrum) with authentic material. *N*-Acetyl-tri-*O*-acetylconduramine C 4 (III) (m. 165°) (1.8 g.) in 30 cc. H_2O and 30 cc. AcOH treated with 32 cc. 3% H_2O–Br gave 1.7 g. IV, m. 200–2° (EtOH). Acetylation of 41 mg. IV with Ac_2O–C_5H_5N gave 42 mg. pentaacetyl deriv., m. 180–1° (EtOH). Treatment of 6.3 g. *N*-acetyl-tri-*O*-acetylconduramine F 4 (V) (m. 148°) in 100 cc. H_2O and 100 cc. AcOH with 110 cc. 3% H_2O–Br gave 6.4 g. VI, 194°. VI (41 g.) acetylated with Ac_2O–C_5H_5N gave 39 mg. pentaacetyl, deriv. m. 196° (EtOH). Treatment of 3.8 g. *N*-acetyl-tri-*O*-acetylconduramine B 1 (VII) (m. 158°)

43—CARBOHYDRATES

M. L. WOLFROM

Study of kinetics of formaldehyde condensation into sugars with the aid of a high-frequency apparatus. I. L. Orestov (Pharm. Inst., Pyatigorsk). *Zh. Fiz. Khim.* 38(11), 2664–6 (1964)(Russ); cf. Zarinskii and Koshkin, *CA* 53, 5*b*. The kinetics of CH_2O condensation into sugars in the presence of $Ca(OH)_2$ was studied at 40–60° by the change in the current i with time τ in a high-frequency titration bridge-based app. (*loc. cit.*). The i vs. τ plot consisted of 4 sections, a rising section during the 1st 20 min., a horizontal section for about 100 min., a section rapidly descending to a pointed min. at τ in about 215 min., and a final rising section. The mechanism corresponding to each section was considered. Only at the min. was CH_2O absent. A min. before the min. sugars were absent. They appeared in the soln. 1 min. beyond the min. GBJR

Synthesis of mycinose (6-deoxy-2,3-di-*O*-methyl-D-allose). J. S. Brimacombe, M. Stacey, and L. C. N. Tucker (Univ. Birmingham, Engl.). *J. Chem. Soc.* 1964(Dec.), 5391–2(Eng). Mycinose, a sugar component of the antibiotic chalcomycin, has



(I)

been synthesized and its identity with 6-deoxy-2,3-di-*O*-methyl-D-allose (I) confirmed. RCJR

Partial acylation of 3-deoxy-D-*xylo*-hexose dithioacetals. Gerhard Rembarz and Thea Reinhard (Univ. Rostock, Ger.). *J. Prakt. Chem.* 26(1–2), 79–82(1964)(Ger). Acylation of a 3-deoxy-D-*xylo*-hexose dialkyl dithioacetal (I) with a limited amt. of BzCl or *p*-toluenesulfonyl chloride gave a cryst. 6-benzoate (II) or a cryst. 6-*p*-toluenesulfonate (III). Dissolving 0.01 mole I in 50 cc. C_5H_5N, cooling to −15°, adding in 30 min. with stirring a soln. of 1.15 cc. BzCl in 5 cc. C_5H_5N, stirring 8 hrs. at −10°, leaving at 0° 16 hrs. and at 20° 3 hrs., pouring into 200 cc. 10% AcOH previously cooled to 0°, recrystg., when crystals were formed, from $CHCl_3$ and pentane, dissolving sirups formed in $CHCl_3$, washing, and drying the soln. with Na_2SO_4, treating with active C, filtering through kieselguhr, evapg., and recrystg. the residue from $CHCl_3$ and pentane gave the following II [alkyl, % yield, m.p., $[\alpha]_D^{25}$ (C_5H_5N) given]: Me, 25, 125°, 34.7° (*c* 2.27); Pr, 38, 59°, 17.2° (*c* 1.47); Bu, 26, 66°, 28.4° (*c* 2.36). Proof of the structure of II (alkyl = Pr) was realized by shaking 12 hrs. 100 mg. of the compd. with 240 mg. $Pb(OAc)_4$ in 60 cc. abs. C_6H_6, filtering through kieselguhr, evapg. the filtrate *in vacuo* to a sirup, dissolving in MeOH, and chromatographing on paper to obtain a spot identical to that of applied glycoaldehyde benzoate. Sirupy, impure 6-*O*-benzoyl-3-deoxy-D-*xylo*-hexose (IV), $[\alpha]_D^{25}$ 12.6° (*c* 0.61, H_2O), was prepd. in 65% yield by stirring 6 hrs. at 45° 0.01 mole II (alkyl = Pr), 60 cc. Me_2CO, 6 cc. H_2O, 6.0 g. yellow HgO, and 6.0 g. $HgCl_2$, cooling, filtering, and washing the residue with Me_2CO, evapg. the combined filtrate *in vacuo* in the presence of some HgO, extg. the residue four times each with 50 cc. hot H_2O, stirring the combined ext. with 30 g. Wofatit L 150 and 7 g. Wofatit F until a neg. Cl^- test to $AgNO_3$ was obtained, filtering, and evapg. IV was also prepd. from other II. 6-*O*-Benzoyl-3-deoxy-D-*xylo*-hexose phenylhydrazone, m. 120°, $[\alpha]_D^{25}$ 19.4° (*c* 1.23, C_5H_5N), was prepd. in 24% yield from 268 mg. crude IV in 5 cc. EtOH, adding a few drops AcOH, a small granule of NaOAc, and 0.13 cc. $PhNHNH_2$, leaving at room temp. 20 hrs., adding a few drops H_2O, cooling to 0° to crystallize, and recrystg. from EtOH–H_2O. The procedure used for II using equimolar amts. of I and *p*-toluenesulfonyl chloride and recrystg. from MeOH–H_2O or $CHCl_3$–pentane gave the following III [alkyl, % yield, m.p., $[\alpha]_D^{25}$ (C_5H_5N) given]: Me, 28, 121°, 33.1° (*c* 1.66); Pr, 47, 68°, 27.8° (*c* 2.43); Bu, 28, 68°, 28.7° (*c* 2.43). J. M. Sugihara

Phosphorylated sugars. IX. A simple synthesis of 2-deoxy-D-ribose 5-phosphate [2-deoxy-D-*erythro*-pentose 5-(dihydrogen phosphate)]. Patricia Szabo and L. Szabo (C.N.R.S., Villejuif, France). *J. Chem. Soc.* 1964(Dec.), 5139–43(Eng); cf. *CA* 59, 5254*e*, 8849*g*. A simple synthesis of substantial quantities of chem. and enzymically pure 2-deoxy-D-ribose (2-deoxy-D-*erythro*-pentose) 5-(dihydrogen phosphate), starting with 1,2:5,6-di-*O*-isopropylidene-D-glucofuranose and passing through 3-deoxy-D-*ribo*-hexose 6-(dihydrogen phosphate), is described. RCJR

Chemistry of 2,5-anhydro sugars. Synthesis of 1-amino-2,5-anhydro-1-deoxy-D-ribitol. Jacques Defaye and Dov Stephan Gero (C.N.R.S., Gif-sur-Yvette, France). *Compt. Rend.* 259 (18), 3121–3(1964)(Fr). From 2,5-anhydro-D-ribitol in acetone in the presence of dry $CuSO_4$ was obtained 2,5-anhydro-3,4-*O*-isopropylidene-D-ribitol (I), $b_{0.005}$ 60–2°, $[\alpha]_D^{25}$ −40.1° (*c* 1.3, MeOH). The *p*-tolylsulfonyl deriv. of I, obtained quant. by treatment of I with *p*-toluenesulfonyl chloride in pyridine, was heated 16 hrs. at 128° with NaN_3 in aq. $MeOCH_2CH_2OH$ to give the 1-azide deriv. of I, $b_{0.005}$ 62–5°, $[\alpha]_D^{25}$ −46° (*c* 0.5, $CHCl_3$), which was quant. hydrogenated in the presence of PtO_2 to yield 1-amino-2,5-anhydro-1-deoxy-3,4-*O*-isopropylidene-D-ribitol (II); 2,4 dinitrobenzene deriv. m. 144.5–5.5° (EtOH), $[\alpha]_D$ −63.6° (*c* 0.42, $CHCl_3$). Aq. HCl hydrolysis of II gave 1-amino-2,5-anhydro-1-deoxy-D-ribitol, m. 164–8°, $[\alpha]_D^{25}$ −79° (*c* 0.442, H_2O). Alfred C. Schram

Chromatographic purification of *N*-acetyl-*N*-D-glucopyranosyl-*p*-aminoazobenzene prepared by the aminolysis of *N*-acetyl-*N*-[2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl]-*p*-aminoazobenzene. Janusz Sokolowski and Zofia Fialkiewicz (Wyzsza Szkola Pedagogiczna, Gdansk, Poland). *Roczniki Chem.* 38(9), 1311–15 (1964)(Pol). A suspension of 2.485 g. *N*-acetyl-*N*-[2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl]-*p*-aminoazobenzene in 250 ml. anhyd. MeOH was treated with a soln. of 0.945 g. Me_2NH (I) in a few ml. MeOH, stirred overnight at room temp., stripped at 15–20 mm. and repeatedly treated with MeOH and stripped to remove unreacted I and $AcNMe_2$. The crude *N*-acetyl-*N*-D-glucopyranosyl-*p*-aminoazobenzene (II) thus obtained was purified by chromatography to give 0.06 g. pure II, m. 115–20°, $[\alpha]_{5800}^{20}$ 48° (*c* 0.5, EtOH). A soln. of 1.64 g. II in 8 ml. C_5H_5N treated at room temp. with 2.8 g. BzCl, kept 24 hrs. at room temp., poured into 250 g. ice-water, and cooled several hrs. gave 0.9 g. *N*-acetyl-*N*-[2,3,4,6-tetra-*O*-benzoyl-D-glucopyranosyl]-*p*-aminoazobenzene, m. 169–71°, $[\alpha]_{5800}^{20}$ −82.5° (*c* 0.2, EtOH). Pure II (1.64 g.), 3.4 g. PhCHO, and 0.95 g. powd. anhyd. $ZnCl_2$ was shaken 5 hrs. at room temp., then extd. successively several times with cold H_2O and petr. ether. The residue after evapn. was powd. and washed with aq. $NaHCO_3$ and H_2O to give 1.7 g. *N*-acetyl-*N*-[4,6-*O*-benzylidene-D-glucopyranosyl]-*p*-aminoazobenzene (III), m. 123–30°, $[\alpha]_{5800}^{20}$ 0° (*c* 0.5, EtOH). To a cold soln. of 0.196 g. III in 3 ml. C_5H_5N, 3 ml. Ac_2O was added at 0°, the whole left 24 hrs. at room temp., then poured into 50 g. ice-water, to afford 0.21 g. *N*-acetyl-*N*-[4,6-*O*-benzylidene-2,3-di-*O*-acetyl-D-glucopyranosyl]-*p*-aminoazobenzene, m. 137–40° (MeOH), $[\alpha]_{5800}^{20}$ −147° (*c* 0.15, EtOH). W. Sobotka

Novel synthetic approach to the ylidene derivatives of carbohydrates. E. Bergonzi, R. Bernetti, C. Boffi, V. Brocca, and E. A. Cleveland (Corn Prod. Co., Argo, Ill.). *Staerke* 16(12), 388–92(1964)(Eng). Cyclic acetals were prepd. from D-glucose (I) and Me α-D-glucopyranoside (II) in Me_2SO with $BF_3.Et_2O$ catalyst. Under the same conditions, ketones did not react. II (0.2 mole), 0.6 mole EtCHO, and 2 ml. $BF_3.Et_2O$ in 200 ml. Me_2SO was stirred 7 hrs. at 65° to give 2 g. Me 2,3-*O*-oxidodipropylidene-4,6-*O*-propylidene-α-D-glucopyranoside, m. 138–9°, $[\alpha]_D^{25}$ 72.2° ($CHCl_3$), and 35 g. Me 4,6-*O*-propylidene-α-D-glucopyranoside, m. 98–100°, $[\alpha]_D^{25}$ 118.2° ($CHCl_3$). Similarly was obtained Me 4,6-*O*-laurylidene-α-D-glucoside, m. 75–6° (MeOH), $[\alpha]_D^{25}$ 77.6° (EtOH), which with Ac_2O in C_5H_5N gave a diacetate, m. 45–6° (EtOH–H_2O), $[\alpha]_D^{25}$ 87.5° (EtOH). From I was obtained 4,6(?)-*O*-propylidene-D-glucose, m. 158–60° (EtOAc), $[\alpha]_D^{25}$ 4.3° (at equil., H_2O), and 4,6(?)-*O*-laurylidene-D-glucose, m. 136° (Me_2CO), $[\alpha]_D^{25}$ 36° (EtOH). 1,2-*O*-Isopropylidene-α-D-glucofuranose was obtained in 20% yield from 0.05 mole I, 0.1 mole Me_2CO, and 0.1 mole $BF_3.Et_2O$ in 50 ml. dioxane at 62° for 1 hr. Similarly, 1,2-*O*-trichloroethylidene-D-glucofuranoses were prepd. in 80.8% yield (58.2% α and 22.6% β isomer). Frederick W. Parrish

Aminolysis of sucrose. IV. Reaction of sucrose with aqueous solution of ethylenediamine. Ivan Jezo and Ivan Luzak (Slovak Acad. Sci., Bratislava, Czech.). *Chem. Zvesti* 18(3), 186–98(1964)(Slo); cf. *CA* 61, 2039*a*. The aminolysis of sucrose was carried out with an aq. soln. of ethylenediamine. The following compds. were isolated and identified: 2-methyl-2-imidazoline, 2-ethyl-2-imidazoline, 2-hydroxy-6,7-dihydro-8-azaquinolizine, piperazino[*a*]-3-hydroxy-8-azaquinolizidine and piperazino-[*a*]-3-hydroxy 8-aza-$\Delta^{8,9(9,10)}$-dehydroquinolizidine. A reaction mechanism is proposed. Karel Kriz

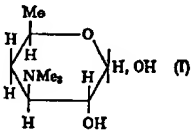
Preparation and use of β-cyanoethylated polyhydric alcohols in gas chromatography. J. Ratusky and L. Bastar (Ceskoslov. Akad. Ved, Prague). *Collection Czech. Chem. Commun.* 29 (12), 3066–80(1964)(Ger). Addn. of CH_2:CHCN (I) to polyhydric alcs. was modified to avoid the undesired formation of polyacrylonitrile. The polyhydric alc. was heated with a catalytic amt. of NaOEt at 100° under simultaneous removal of EtOH. The resulting partial alkoxide was treated dropwise with I (at the reflux temp. of I) to give a low-melting mixt. of the starting polyhydric alc. with the partially β-cyanoethylated polyhydric alc. The temp. of the resulting homogeneous mixt. was then lowered and the remaining I was added. Thus, 24.2 g. finely powd. erythritol was stirred at 100° with 1.1 g. NaOEt, the EtOH being simultaneously distd., the residue treated dropwise in 5 min. at 80° with 15 ml. I and then in 45 min. at 60° with 37 ml. I, the whole kept overnight at room temp., decompd. with 100 ml. H_2O, the suspension washed with CH_2Cl_2, the ppt. collected, and

CAOLD answer # 2

the filtrate extd. with CH_2Cl_2 (the CH_2Cl_2 exts. were evapd. and the residues β-cyanoethylated once more). The ppt. was purified by chromatography over neutral Al_2O_3 or by crystn. to give 1,2,3,4-tetrakis(β-cyanoethoxy)butane (II), m. 106–8° (MeOH). Similarly were prepd. the per(β-cyanoethyl) ethers of glycerol (ether $b_{0.1}$ 234–7°), D-glucitol, D-mannitol, diglycerol, and pentaerythritol (ether m. 48–51°). II was successfully used as the stationary phase in gas chromatography to sep. various position isomers (e.g., isomeric xylenes, cresols, Me toluates, $C_{10}H_7CO_2Me$, $C_6H_4(CO_2Me)_2$, $C_6H_3(CO_2Me)_3$, Me pyridinecarboxylates, $O_2NC_6H_4CN$, $C_6H_4(NO_2)_2$, $C_6H_4(OH)_2$, $HOC_6H_4CO_2Me$, HOC_6H_4CN, $HOC_6H_4NO_2$, $MeOC_6H_4NO_2$, $H_2NC_6H_4NO_2$, $MeNHC_6H_4NO_2$, $Me_2NC_6H_4NO_2$) and stereoisomers (cis and trans cycloolefins and Me cycloalkanolcarboxylates, 2-methyl-4-*tert*-butylcyclohexanols, 5-*tert*-butyl Me-2-hydroxycyclohexanecarboxylates). Finely ground unglazed tile was used as an inert support. Jiri Pliml

Synthesis and investigations of glycosylamines and attempts at glycosidation of *p*-aminothiophenol. Jerzy Sykulski (Akad. Med., Lodz). *Acta Polon. Pharm.* 20(2), 131–40(1963)(Pol). The effect of the SH group on glycosylation of amines was investigated with *p*-$H_2NC_6H_4SH$ (I) derivs. as model substances. The procedure was essentially that of Weygand (*CA* 34, 83[8]). Attempts at glycosidation of PhSH and *p*-$AcNHC_6H_4SH$, with or without HCl as catalyst, were neg. The following glycosylamines were prepd. from I [sugar component, m.p., $[\alpha]_D$/temp. (*c* 1, C_5H_5N), and R_f value ascending chromatography in 2:1:3:2 BuOH–C_6H_6–C_5H_5N–H_2O given]: D-glucose, 122–5°, −120.4°/25.5°, 0.96; D-galactose, 154–6°, −123.3°/21°, 0.61; D-mannose, 159–62°, −197.2°/21°, 0.67; L-rhamnose, 153–6°, 196.9°/21°, 0.81; lactose, 196–8°, −49.5°/19°, 0.64; maltose, 140–50°, —, 0.72; L-arabinose, — (oil), —, 0.64; D-arabinose, — (oil), —, 0.68; D-ribose, — (oil), —, 0.69; D-xylose, — (oil), —, 0.68. For a glycosylamine prepd. from D-glucose and *p*-H_2N-C_6H_4SMe, the corresponding data were 172–5°, —, 0.68, resp. All the compds. gave pos. color reactions for the SH group. *N*-(*p*-Mercaptophenyl)-D-glucosylamine (II) (1 g.) in 8 ml. C_5H_5N left 3 days at room temp. with 6 ml. Ac_2O yielded 0.73 g. penta-*O*-Ac deriv. of II, m. 148–50°. The penta-*O*-Bz deriv. of II, m. 195–8°, was prepd. similarly with BzCl. II had no reducing properties [test with *o*-$C_6H_4(NO_2)_2$], showing it to be a D-glucosylamine and not the isomeric Amadori rearrangement product. II (1 g.) dissolved in 15 ml. 5% NaOH, the soln. shaken with 7 ml. Me_2SO_4, acidified with HCl, refluxed 30 min., alkalized, extd. with Et_2O, the ext. evapd., and the residue refluxed with 3 ml. Ac_2O and poured on ice gave 0.01 g. *p*-$AcNHC_6H_4SMe$, m. 128.5–9.7° (C_6H_6). The SH group in I was considered to have no catalytic effect on I glycosylamination. Jerzy Lange

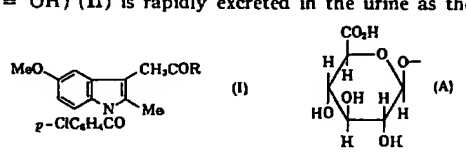
The synthesis of desosamine hydrochloride. A. C. Richardson (Univ. Bristol, Engl.). *J. Chem. Soc.* 1964(Dec.), 5364–70 (Eng). By use of Me 3-acetamido-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranoside as starting material, 3,4,6-trideoxy-3-dimethylamino-D-*xylo*-hexose (I) hydrochloride has been synthesized; it is identical with the naturally occurring sugar desosamine hydrochloride. RCJR



(I)

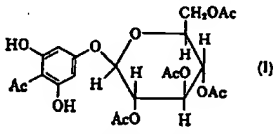
Sorboses. V. Reactions of the *p*-tolylsulfonyloxy groups of 2,3-*O*-isopropylidene-α-L-sorbofuranoses in liquid ammonia. Kanji Tokuyama (Shionogi Co., Ltd., Osaka). *Bull. Chem. Soc. Japan* 37(8), 1133–7(1964)(Eng); cf. *CA* 61, 13394*f*. The reactions of *p*-tolylsulfonyl groups in liquid NH_3 were extended to $NaNH_2$, KCN, KSCN, NaOH, and NaSH with the following results: in the absence of a solute 2,3:4,6-di-*O*-isopropylidene-1-*O*-*p*-tolylsulfonyl-α-L-sorbofuranose in liquid NH_3 gave only the 1,1′-bis(amine); KCN gave an amidine which was hydrolyzed to the 1-carboxamide, $[\alpha]_D^{25}$ −4.8° (*c* 1.011, $CHCl_3$); KSCN gave only the 1-amine; NaSH gave mercaptans or sulfides, depending on conditions; otherwise normal substitution occurred. Chilton H. McDonnell

Synthesis of indomethacin metabolites. R. G. Strachan, M. A. P. Meisinger, W. V. Ruyle, Ralph Hirschmann, and T. Y. Shen (Merck Sharp Dohme Labs., Rahway, N.J.). *J. Med. Chem.* 7(6), 799–800(1964)(Eng); cf. *CA* 60, 15005*c*. In man, the new non-steroidal antiinflammatory agent, indomethacin (I, R = OH) (II) is rapidly excreted in the urine as the acyl glucuronide (I, R = A) (III). The chem. lability of acyl glucuronides is well known and facile hydrolytic cleavage of the glucoside linkage of III was observed during isolation. The *N*-aryl group was readily removed under mildly acidic or alk. conditions and *in vivo* diacylation gave the known acid. Preferential demethylation in C_5H_5N.HCl at 180° yielded the *O*-demethyl analog. II K salt condensed with Me 2,3,4-tri-*O*-acetyl-1-bromo-1-deoxy-α-D-glucuronate in MeOH yielded I (R = 2,3,4-tri-*O*-acetyl deriv. of A) (IV). Exploratory attempts to convert V into III were unsuccessful. The *in vivo* metabolite III (from rabbit urine) was esterified and acetylated to give IV, thus establishing the structure of III. C. R. Addinall



(I) (A)

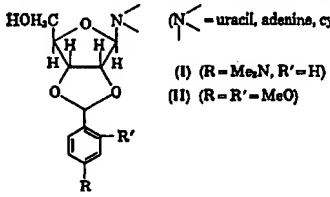
Synthetic studies of flavonoids. V. Synthesis of eryodictiol 7-β-D-glucoside and its methyl ether. N. B. Tarusova, A. N. Vetrov, and N. A. Preobrazhenskii (M. V. Lomonosov Inst. Fine Chem. Technol., Moscow). *Zh. Obshch. Khim.* 34(10), 3300–3 (1964); cf. *CA* 58, 12500*h*. Reaction of I in MeOH–60% aq. KOH at 1–2° with $3,4\text{-}(HO)_2C_6H_3CHO$ under N atm. gave in 1.5 days 42.7% 2′,3,4,4′,6′-pentahydroxychalcone 4′-β-D-glucopyranoside, m. 194–6°, which in 50% aq. MeOH heated with phosphate buffer (pH 7) 15 min. at 90° and kept 18 hrs. at 4–5° gave 3′,4′,5,7-tetrahydroxyflavanone 7-β-D-glucopyranoside dihydrate (II), m. 196–7°. I and isovanillin gave 52.5% 2′,3,4′,6′-tetrahydroxy-4-methoxychalcone 4′-β-D-glucopyranoside, m. 178–80° (contg. 4.5 moles H_2O), which was converted into 72% 3′,5,7-trihydroxy-4′-methoxyflavanone 7-β-D-glucopyranoside dihydrate, m. 249–50°, which in 1 hr. at 90–5° in 10% H_2SO_4 gave 98.1% 3′,5,7-trihydroxy-4′-methoxyflavanone, m. 228–9°, also formed by similar treatment of neohesperidine in 77% yield. Uv and ir spectra were reported. II was identical with eryodictiol 7-glucoside. G. M. Kosolapoff



(I)

Synthesis of coenzyme A. A. M. Michelson (Arthur Guinness Son and Co. Ltd., Dublin, Ire.). *Biochim. Biophys. Acta* 93 (1), 71–7(1964)(Eng). An improved procedure for the chem. synthesis of coenzyme A by anhydride-anion exchange was described. A mixt. of the 2′,5′- and 3′,5′-diphosphates of adenosine was treated with diphenylphosphorochloridate to give P^1-adenosine (2′,3′-cyclic phosphate)-5′-P^2-diphenyl pyrophosphate quant. This was treated with pantethine 4′,4′-bisphosphate in C_5H_5N to give a 2′,3′-cyclic phosphate form of coenzyme A with displacement of diphenyl phosphate from the intermediate mixed anhydride. Specific enzymic opening of the cyclic phosphate gave coenzyme A in high yield. A synthesis of guanosine 2′(3′),5′-diphosphate was also described. RCCF

Substituted 2,3-benzylidene ribonucleosides. Friedrich Cramer, Wolfram Saenger, Karl Heinz Scheit, and Juergen Tennigkeit (Tech. Hochschule, Darmstadt, Ger.). *Ann.* 679, 156–63(1964)(Ger). The prepn. of 2′,3′-*O*-(4-dimethylaminobenzylidene) (I) and 2′,3′-*O*-(2,4-dimethoxybenzylidene) ribonucleosides (II) was described. These compds. were hydrolyzed under mild acid conditions and could be phosphorylated with 2-cyanoethyl phosphate (III) (Tener, *CA* 55, 24771*g*) and dicyclohexylcarbodiimide (DCC). After cleavage of the protective groups, nucleoside 5′-phosphates were obtained exclusively. Uridine (2 millimoles), 5 millimoles $4\text{-}Me_2NC_6H_4CHO$, 4 cc. dioxane, and 18 millimoles CF_3CO_2H (IV) or CCl_3CO_2H (V) heated slightly in a closed vessel, and the homogeneous liquid shaken 24 hrs. at room temp. and worked up gave 67% 2′,3′-*O*-(4-dimethylaminobenzylidene)uridine, m. 203–4° (H_2O contg. a little EtOH). From cytidine was similarly prepd. 78% 2′,3′-*O*-(4-dimethylaminobenzylidene)cytidine (VI), m. 209–10° (H_2O). From adenosine was prepd. 69% 2′,3′-*O*-(4-dimethylaminobenzylidene)adenosine, m. 218–20° (H_2O contg. a little EtOH). With guanosine, the reaction did not proceed to completion; work-up gave 0.4 g. 2′,3′-*O*-(4-dimethylaminobenzylidene)guanosine, m. 269–70°. VI (2.5 millimoles) in 10 cc. $HCONMe_2$ (DMF) was treated as described for N^6-benzoyl-2′,3′-*O*-(dimethoxybenzylidene)cytidine (VII) (see below) and worked up (chromatography) to give 69% N^4-benzoyl-2′,3′-*O*-(4-dimethylaminobenzylidene)cytidine (VIII), m. 173–5° ($CHCl_3$-petr. ether) (MeOH); sometimes VIII crystd. as VIII.H_2O, m. 124–6°. In

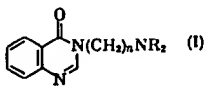


(N = uracil, adenine, cytosine, guanosine)

(I) (R = Me_2N, R′ = H)

(II) (R = R′ = MeO)

give the base hydrochloride, which was hygroscopic and crystd. from abs. EtOH-ether (yield 20%). Following II were prepd. (R, *n*, and m.p. or b.p. given): Et, *2*, b_2 200–2°; Pr, *3*, m. 190–1° (softened at 165°) (hygroscopic, isolated as hydrochloride); Bu, *2*, b_4 222–5°; and Et, *3*, b_3 210–14°. I (1 mole) in dry C_6H_6 or xylene (20 ml.) was treated with the appropriate alkyl or aryl halide (1 mole) and the mixt. refluxed (4–24 hrs.) to give the quaternary salt (III); this was filtered off, washed (dry C_6H_6) and dried *in vacuo*. The following III were prepd. (R, R^1, X, *n*, and m.p. given): Me, allyl, Br, *3*, 225–7°; Me, Me, I, *2*, 270° (decompn.); Me, Et, I, *2*, 228–9° (decompn.); Me, Pr, I, *2*, 178–80°; Me, benzyl, Br, *2*, 148–9° (sepd. with $2H_2O$); Me, Bu, I, *2*, 160–1°; Me, *p*-nitrobenzyl, Br, *2*, 227–9° (decompn.); Me, β-phenylethyl, Br, *2*, 202–3°; Et, Me, I, *2*, 152–5° (decompn.); Et, benzyl, Br, *2*, hygroscopic; Pr, Me, I, *2*, 170–2°; Pr, benzyl, Br, *2*, 148–50°; Pr, *p*-nitrobenzyl, Br, *2*, 204–5° (decompn.); Bu, Me, I, *2*, 160° (decompn.) (softened at 143°); iso-Bu, Me, I, *2*, 154–5°; Et, Me, I, *3*, 133–5°; Et, Et, I, *3*, 111–12°; Et, benzyl, Br, *3*, hygroscopic; Et, *p*-nitrobenzyl, Br, *3*, 205–6°; Bu, benzyl, Br, *3*, hygroscopic; and Bu, *p*-nitrophenyl, Br, *3*, 78–9°. Some of the compds. reported possessed pronounced spasmolytic activity.



(I)

V. K. Ahluwalia

2,5-Dimethylpiperazine synthesis from 1-amino-2-propanol. W. K. Langdon, W. W. Levis, Jr., and D. R. Jackson (Wyandotte Chemicals Corp., Wyandotte, Mich.). *Ind. Eng. Chem.* 1, No. 2, 153–6(1962). In the presence of Raney Ni catalyst (I) and H, 1-amino-2-propanol (II) undergoes a bimol. cycloamination yielding 2,5-dimethylpyrazine (III), *trans*-2,5-dimethylpiperazine (IV), and *cis*-2,5-dimethylpiperazine (V). I and II are charged into a 1-l. stainless steel autoclave in such amts. that there are 2.5 g. of I per mole of II. The autoclave is then flushed several times with N and then with H. H is admitted to 1200 lb./sq. in. and the mixt. rapidly heated to 220° venting H to maintain 1200 lb./sq. in. The mixt. is agitated 4–8 hrs., cooled to 80°, the H released, and 200 ml. H_2O added. I is removed by filtration through Celite and the filter cake washed with H_2O. V is removed as an azeotrope with water, b. 98°, through a 2.8 × 120 cm. packed column with a reflux ratio between 2:1 and 5:1. IV and V were distd. at 155–70°. There is a 75% yield of a mixt. of 80% IV and 20% V. The following changes in reaction variables all resulted in greater yields of IV and V: increasing temp. from 180 to 220°, increasing H pressure from 200 to 1200 lb./sq. in., increasing reaction time from 2 to 8 hrs., and increasing g. of I per mole of II from 0.6 to 2.5. Thomas E. Whiteley

Condensation reaction of amino alcohols with imides. IV. Condensation products of β-(cycloamino)ethanols with succinimide and with phthalimide—formation of β-(cycloamino)ethylamines. Kazuo Nakajima (Teikoku Chem. Ind., Mibukayogosho, Kyoto). *Nippon Kagaku Zasshi* 81, 1129–32(1960); cf. *CA* 57, 8545*h*. Seven aminoalcs. ($RNCH_2CH_2OH$) (I), where RN = $(CH_2)_4N$ (*a*), $(CH_2)_5N$ (*b*), β-tetrahydroquinoline (*c*), morpholino (*d*), 4-ethylpiperazino (*e*), 4-butylpiperazino (*f*), and 4-phenylpiperazino (*g*). I and phthalimide heated at 200° while removing the H_2O formed yielded $RNCH_2CH_2N(CO)_2C_6H_4$-*o* (II) (RN, m.p., b_{10}, m.p. of picrate, and decompn. point of Pt salt given): *a*, 109°, 220°, 218°, 212°; *b*, 90°, 206°, 215°, 215°; *c*, 137°, 273°, 144°, 204°; *d*, 135°, 216°, 232°, 146°; *e*, 115°, 227°, 245° (decompn.), 265°; *f*, 75°, 252°, 260° (decompn.), 271°; *g*, 158°, 279°, 218° (decompn.), 262°. Similarly, I and succinimide yielded $RNCH_2CH_2N(COCH_2)_2$ (III) (RN, m.p., b_{10}, m.p. of picrate, and decompn. point of Pt salt given): *a*, 55°, 170°, 158°, 212°; *b*, —, 170°, 190°, 230°; *c*, 115°, 210°, 180°, —; *d*, 75°, 170°, 181°, 175°; *e*, —, 199°, 245°, 245°; *f*, 65°, 223°, 225°, 255°; *g*, 141°, 272°, 175°, 236°. II and III refluxed with 20% HCl 3–5 hrs., phthalic acid or succinic acid filtered off, and the filtrate concd. yielded $RNCH_2CH_2NH_2$.HCl (IV.HCl). Free $RNCH_2CH_2NH_2$ (IV) was obtained by a long extn. of neutralized IV.HCl with ether. (RN, b_{10}, b_{750}, m.p. of picrate, and decompn. point of Pt salt given) *a*, 33°, 165–6°, 210° (decompn.), 207°; *b*, 50°, 185°, ~200 (decompn.), 218°; *c*, 157°, 290°, —, —; *d*, 81°, 204°, 177° (decompn.), 237°; *e*, 88°, 223–4°, 230°, 270°; *f*, 120°, 255°, 116°, 252°; *g*, (m. 80°), 191°, 326°, —, 210–40°. H. Kubo

Synthesis of potential anticancer agents. XXX. (1-Aziridinyl)purines. J. A. Montgomery, K. Hewson, and C. Temple, Jr. (Southern Res. Inst., Birmingham, Ala.). *J. Med. Pharm. Chem.* 5, 15–24(1962); cf. *CA* 56, 1445*a*. Eight (1-aziridinyl) purines were prepd. by nucleophilic displacement of the Cl in the corresponding chloropurines. The compds. were screened against Ca 755 and Walker 256, and the 6-(1-aziridinyl)purines show moderate activity against the Ca 755, and in 1 case good activity against Walker 256. 6-(1-Aziridinyl)-9-benzyl-9*H*-purine (I) (100 mg.) in 10 ml. EtOH was hydrogenated at room temp./atm. pressure with 50 mg. 5% Pd–C catalyst 18 hrs., the catalyst filtered off, the filtrate evapd. to dryness, the residue dissolved in 10 ml. 0.1*N* HCl, the soln. evapd. to dryness *in vacuo*, the residue triturated with 10 ml. Me_2CO, the ppt. filtered off, and dried *in vacuo* to give 90 mg. 9-benzyl-N^6-ethyladenine-HCl. I can also be reduced with metallic Na in liquid NH_3 to give N^6-ethyladenine, m. 227–8° (decompn.). A mixt. of 5.7 g. 2,6-dichloropurine, 6.9 ml. benzyl chloride, 4.2 g. K_2CO_3, and 50 ml. Me_2SO was stirred 18 hrs., filtered, the filtrate concd. to one-quarter vol. *in vacuo*, poured into ice-H_2O, the oil allowed to solidify, filtered, washed with H_2O, air dried, and recrystd. from 75% aq. EtOH with Norit treatment to give 5.9 g. of a mixt. of the 7- and 9-isomers of benzyl-2,6-dichloro-9*H*-purine, m. 122–30°. Recrystn. from MeOH gave 1.06 g. pure 9-isomer, m. 148°. The mother liquors from the recrystn. gave 30% yield of the 7-isomer, contaminated with the 9-isomer. Prepd. similarly was 2-amino-9-benzyl-6-chloro-9*H*-purine, and 2-amino-7-benzyl-6-chloro-7*H*-purine. 9-Benzyl-2,6-dichloropurine (278 mg.) in 10 ml. 0.2*N* NaOH was refluxed with stirring to effect soln., the hot mixt. filtered, the filtrate acidified with glacial HOAc, the ppt. filtered off, washed with dil. HOAc, and dried *in vacuo* to give 233 mg. 9-benzyl-2-chlorohypoxanthine (II), m. 245°. II (100 mg.) in 15 ml. abs. EtOH was placed in a glass-lined Parr bomb, satd. with dry NH_3 at 5°, the soln. heated 6 hrs. at 150°, the bomb chilled, opened, the soln. concd. to 10 ml. in a stream of dry N, the solid filtered off, washed with EtOH, and dried *in vacuo* to give 53 mg. 9-benzylguanine (III), m. 303°. III may also be prepd. from 2-amino-9-benzyl-6-chloropurine by reaction with HCl. II (0.29 millimole) and 0.2 ml. 25% aq. dimethylamine were dissolved in 10 ml. dioxane, the mixt. heated 20 hrs. at 95–100°, with an addn. of another quantity of Me_2NH at the end of the first 2 hrs., the mixt. evapd. to dryness *in vacuo*, the residue triturated with Et_2O, and the residue recrystd. from EtOH to give 57 mg. 9-benzyl-N^2,N^2-dimethylguanine, m. 282°. 7-Benzyl-2,6-dichloropurine (contaminated with the 9-isomer) (1.11 g.) in 25 ml. *N* NaOH was heated 1.5 hrs. at 115°, cooled to room temp., kept overnight in the refrigerator, the solid filtered off, dissolved in H_2O, acidified with glacial HOAc, the solid filtered off, dried *in vacuo*, and recrystd. from abs. EtOH to give 60 mg. 7-benzyl-2-chlorohypoxanthine, m. 285°. 6,8-Dichloropurine (1.06 g.), 0.60 g. anhyd. K_2CO_3, and 1.4 ml. $PhCH_2Cl$ in 10 ml. $HCONMe_2$ was heated 1 hr. at 70–85° with stirring, concd. to 0.5 vol. *in vacuo*, poured into ice-H_2O, the oil extd. with Et_2O, the ext. dild. with EtOH, the solid filtered off, washed with Et_2O, dried, extd. with Skellysolve C, the ext. evapd. to an oil, dissolved in 1:1 aq. EtOH, the solid filtered off, washed with H_2O, dried *in vacuo* over P_2O_5 at room temp., and recrystd. from aq. EtOH to give 203 mg. 9-benzyl-6,8-dichoro-9*H*-purine, m. 92°. Prepd. by similar methods was 9-benzyl-6-dimethylamino-9*H*-purine, m. 117°. 9-Benzyl-6-dimethylamino-8-chloropurine (307 mg.), 43 mg. MgO, and 34 mg. 5% Pd–C in 30 ml. abs. EtOH was hydrogenated at atm. pressure 6 hrs., the catalyst filtered off, the filtrate evapd. to dryness, and the residue triturated with EtOH to give 135 mg. 9-benzyl-6-dimethylaminopurine, m. 128°. Aletha Kowitz

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See also: Identification and detn. of *o*-phenylenediamine in residual waters, in the synthesis of 2-sulfanilamidoquinoxaline (sulfaquinoxaline), by paper chromatography (Sterescu) 24. Mechanism of the aminonitrile rearrangement (Ioffe) 27. Reaction of 2,3-dihydrofurans with 2,4-dinitrophenylhydrazine (Boberg) 31. Kinetics of the reversible hydration of 2-hydroxypteridine (Inoue) 5. Nucleic acid components and their analogs—synthesis of 3-methyl-6-azauridine 5′-phosphate and pyrophosphate (Zemlicka) 37.

Univ.). *Vitamins* (Kyoto) 10, 353–9(1956).—*S*-Acetylthiamine diphosphate (I) was synthesized by the acetylation of cocarboxylase in alk. medium with Ac_2O. The *S*-acetyl group in this compd. underwent transacetylation with cysteine as well as glutathione in aq. media. The hydrolysis of I in the presence of chicken liver or pigeon breast muscle homogenate was greatly promoted by the addn. of glutathione. Hiroyasu Fukuba

Reduction of the *aci*-reductone hydroxycomenic acid; peroxidative effects of yeast nucleic acid and adenine. Hans v. Euler and Hans Hasselquist (Univ. Stockholm). *Ann.* 604, 41–7(1957).—Meconic acid (1 g.) in 10 cc. 6% HBr soln. heated 3 hrs. on a steam bath, the mixt. cooled to 0° and treated carefully with 0.3 cc. Br, the suspension of bromocomenic acid heated on a steam bath, the cooled soln. extd. with EtOAc, the dried ext. concd., and the cryst. product recrystd. from EtOAc gave hydroxycomenic acid (I), m. 243°, reducing Tillmans reagent, iodine soln., and giving a red-violet ppt. with 2,3,5-triphenyltetrazolium chloride; Et ester, reducing Tillmans reagent. I (0.3 g.) in 5 cc. H_2O shaken with 11.4 cc. soln. (4.5 g. Br in 100 cc. $CHCl_3$), the aq. layer washed with $CHCl_3$ and extd. with EtOAc, the filtered ext. dried and evapd., and the residue crystd. from EtOAc gave 80 mg. brown prisms of a bromo compd., $C_5H_3BrO_5$, purified by recrystn. to a pure material, m. 120° [hardening and melting sharply at 170° (decompn.)]. In connection with the effect of I in combination with chemotherapeutic agents on rat sarcoma, *in vitro* expts. on peroxidase systems were reported. Pyrogallol (15 mg.), 0.5 cc. 6% H_2O_2, and 5 cc. buffer soln. (pH 6.8) at 20° in 30 min. gave a min. amt. of purpurogallin (II) ($E_{1\,cm.}$ 0.002). Addn. of 30, 15, 7.5 mg. yeast nucleic acid per cc. of above reaction mixt. gave 2.12, 1.02, 0.66 mg. II ($E_{1\,cm.}$ 0.06, 0.03, 0.017) corresponding to 7.1, 6.8, 8.8 mg. II per 100 mg. nucleic acid. Addn. of 5.0, 2.5, 1.25 mg. adenine to the mixt. gave 64.2, 64.4, 67.1 mg. II per 100 mg. adenine. Test of cleavage products of yeast nucleic acid and other purine and pyrimidine bases showed only adenosine and adenosine phosphoric acid to have equiv. activity to adenine. Guanine and uracil have much less activity. Of the amino acids only *p*-$H_2NC_6H_4CO_2H$ was significantly active. Xanthine, clupeine, theophylline, tyrosine, and suprarenin proved inactive. Pyrogallol (150 mg.) in 30 cc. H_2O, 10 cc. phosphate buffer (pH 6.8), 1 cc. 6% H_2O_2, and 1 cc. yeast emulsion warmed 10 min. at 20, 50, 56, 60, and 69 gave relative peroxidase effects of 6.9, 8.0, 18.2, 10.2, and 0.7, confirming previous findings (cf. E. and Blix, *C.A.* 13, 3210) that the effect of catalase is increased 3–4 fold by warming to 56°. C. R. Addinall

Chemotherapeutic studies in the heterocyclic series. XVIII. Polymethylenedi(sydnones) and polymethylenedi(hydrazines). H. U. Daeniker and J. Druey (Ciba A.-G., Basel, Switz.). *Helv. Chim. Acta* 40, 918–32(1957), cf. *C.A.* 51, 10518*b*.—A mixt. of $[(CH_3)_nNH_2]_2$, CH_2O, and HCN or KCN forms with HNO_2 followed by boiling with KOH the following $[(CH_3)_nN(NO)CH_2CO_2H]_2$ (I) (*n* and m.p. given): *1*, 143.5–5.0°; *2*, 142°; *3*, 126–7°. I and Ac_2O or $(CF_3CO)_2O$ form the di(sydnones) (II) $[(CH_2)_nN.N.O.CO.CR]_2$ (R = H) which can be halogenated with a hydrohalic acid and halate to II (R = Cl or Br). The following II are reported (*n*, R, and m.p. given): *1*, H, 169°; *1*, Cl, 120–30° (explodes); *1*, Br, 163° (explodes); *2*, H, 170°; *3*, H, 114–16°; *3*, Br, 120–2°. II (*n* = 1, R = Me), decomp. 182–3°, λ 300 mμ (ε 15,800), is prepd. using AcH via $[CH_2N(NO)CHMeCO_2H]_2$, m. 164–5°. II with HCl in MeOH form the following $[(CH_3)_nNHNH_2.HCl)]_2$ (III) (*n* and m.p. given): *1*, 160°; *2*, 156–60°; *3*, 139–41°. III (*n* = 3) and BzH form the dihydrazone (IV), m. 80°, but III (*n* = 1 or 2) form compds. m. 132–3° and 154–5°, resp., in which a third benzylidene group bridges the 2 central N atoms. These compds. lack any absorption in the 3 μ region characteristic of NH vibrations. IV absorbs as expected at 2.93 μ. III (*n* = 1) and 3 moles *o*-HOC_6H_4CHO form an analogous cyclic dihydrazone, m. 190°. III and *o*-$C_6H_4(CHO)_2$ form 2,2′-polymethylenebis(phthalazinium salts) $[(CH_2)_nC_8H_6N_2.Y]_2$ (V). V (*n* = 1, Y = Br) was also prepd. from phthalazine and $(CH_2Br)_2$. The following V are reported [*n*, Y, m.p., and λ in mμ (ε) given]: *1*, Cl, 221°, 311 (7800), 282 (7600), 233 (41,000); *1*, Br, 277–8°, 310 (8400), 280 (8050), 234 (52,400); *2*, Cl, 285–6°, 318 (7200), 278 (6800), 234 (51,000); *3*, Cl, 248°, 318 (6900), 278 (6500), 234 (60,000). V (*n* = 2, Y = Cl) and alkali form an impure 2,2′-tetramethylenedi(1-hydroxy-1,2-dihydrophthalazine), m. 164°. V (*n* = 1) forms instead the cyclic anhydride of the analogous compd., m. 150–2°, λ 308 (17,800), 234 mμ (17,750), 6.22, 6.47, and 6.73 μ but no OH band in the 3 μ region. 1-Hydroxy-2-butyl-1,2-dihydrophthalazine, prepd. for comparison, m. 67–8°, λ 310 (8850), 234 mμ (15,500), 2.81 μ. Acidification of all of these compds. reforms V. *N*-Butylphthalazinium chloride m. 64–84°, λ 318 (3200), 277 (3200), and 234 mμ (36,000). II and III (*n* = 1, R = H or halogen) weakly inhibit the *in vivo* formation of tumors and are nontoxic. J. H. S.

Structure of proteins. IV. Progressive degradation of the polypeptide chain at the *N*-terminal amino acid. I. Formation of 7-nitro-3,4-dihydro-2-hydroxyquinoxalines. Ernesto Scoffone, Elio Vianello, and Alberto Lorenzini (Univ. Padua). *Gazz. chim. ital.* 87, 354–65(1957); cf. *C.A.* 51, 13955*a*.—An improved method of identification of amino acids is given. The 2,4-dinitrophenyl deriv. is suspended in 6 ml. 95% EtOH and heated with 6 ml. concd. $(NH_4)_2S$ 30 min. at 45–50° to give the *2-amino-4-nitrophenyl deriv.* This is cyclized by acidification to pH 2–3 and heating 15 min. at 70° to *7-nitro-3,4-dihydro-2-hydroxyquinoxaline* (I) or its 3-substitution product. The method is preferable to that of complete reduction with Pt-H to the 7-amino compds. (Jutisz and Ritschard, *C.A.* 50, 4052*i*), which are sensitive to air-oxidation. The m.ps. of the dinitrophenyl derivs. are: glycine, 191–1.5° (decompn.); alanine, 173–4°; valine, 182–3°; leucine, 131–2°; serine, 186–8°; threonine, 176–7°; aspartic acid, 187–8° (decompn.); glutamic acid, 158–62°; methionine, 108–10°; phenylalanine, 208–10° (decompn.); tryptophan, 195–7° (decompn.). The m.ps. (decompn.) of I and its derivs. are: I, 254–4.5°; 3-Me, 224–5°; 3-iso-Pr, 221.5–2.5°; 3-iso-Bu, 217–18°; 3-$HOCH_2$, 221–2°; 3-MeCHOH, 227–7.5°; 3-$HOCOCH_3$, 253–4°; 3-$HOCOCH_2CH_3$, above 280°; 3-$MeSCH_2CH_2$, 213–14°; 3-Bz, 210–11°; 3-(3-indolylmethyl), 220–1°. Data on ultraviolet absorption max. are given, as are R_f values for chromatographic sepn. I is oxidized by alk. $KMnO_4$ to *7-nitro-2-hydroxyquinoxaline* (II), m. 268–9°, and by $K_2Cr_2O_7$ to *7-nitro-2,3-dihydroxyquinoxaline* (III), m. 363–4°. I, II, and III were identified by independent synthesis from 4-nitro-*o*-phenylenediamine and $HOCH_2CO_2H$, $(RO)_2CHCO_2H$, and $(CO_2H)_2$, resp. Richard N. Lewis

Triethylenediamine (1,4-diazabicyclo[2,2,2]octane) and hexaethylenetetramine. III. Interaction of 2,2′,2″-trichlorotriethylamine hydrochloride and dimethylamine. Frederick G. Mann and F. C. Baker (Univ. Cambridge, Engl.). *J. Chem. Soc.* 1957, 1881–99; cf. *C.A.* 50, 358*h*; Hromatka and Kraupp, *C.A.* 46, 8123*i*.—When a mixt. of $(ClCH_2CH_2)_3N.HCl$ (I) and a 40% soln. (3.4 moles) of methanolic Me_2NH (II) is set aside at room temp. 24 hrs. or heated at 45–50° 1.5 hrs. and then treated with HCl, *1-(2′-chloroethyl)-4,4-dimethylpiperazinium chloride hydrochloride monohydrate* (III) is isolated. III is also obtained when the proportion of II is varied from 2.0 to 6.6 moles with the same heating. III, hydrated or anhyd., m. 264° with two well-defined stages of effervescence. An MeOH soln. of III when shaken with Ag_2O and treated with MeI gives the piperazinium iodide in the cold and the iodide methiodide when refluxed. When I is heated with methanolic II (12.8 moles) at 40–5° 8 hrs., the product is *1-(2′-dimethylaminoethyl)-4,4-dimethylpiperazinium chloride-2HCl* (IV), m. 227–8°. When heated with methanolic II (10.7 moles) at 125° 7 hrs., I yields *1-(2′-dimethylaminoethyl)-4-methylpiperazine-3HCl* (V), m. 262° after recrystn., 270° after sublimation. The free base (Va), b_{12} 94°, is liberated by treating V with concd. aq. alkalies. III gave triethylenediamine-HCl methochloride on heating at 250–4°. Due to different results obtained by other workers, the prepn., properties, and identification of triethylenediamine (VI), m. 156–7°, were studied and a no. of derivs. of this and other amines were prepd. The thermal decompn. of IV and V at atm. pressure gives similar products. Thus, using V, distn. of the ethereal exts. of the liberated amines gives the following fractions (1) the ether distillate, contg. 1,4-dimethylpiperazine (VII), b. 131–2°; (2) a fraction, b. 130–3°, of VII contg. a small amt. of piperazine; (3) a large fraction, b_{12} 86–7°, consisting of $Me_2NCH_2CH_2N.(CH_2)_3.NMe.(CH_2)_2$ (VIII), contaminated with a base, $C_8H_{19}N_3$; (4) a small fraction, $b_{0.03}$ 91°, m. 40–3°, which was shown by independent synthesis to be *1,2-*

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bis(4-methyl-1-piperazinyl)ethane (IX), and (5) a small amt. of a fraction, $b_{0.06}$ 105–8°, believed to be *1,4-bis[2-(4-methyl-1-piperazinyl)ethyl]piperazine*. The 4,4′-di-Me deriv. of IX was prepd. by hydrolysis of the 4,4′-bis(ethoxycarbonyl) deriv. followed by H_2CO-HCO_2H methylation of the hydrolysis product. The products of the thermal decompn. of IV differ from those of V only in that fraction 2 contained only a trace of piperazine, fraction 3 is almost pure VIII, and fraction 5 is not detected. Possible errors in earlier literature in the identification of certain of these amines is discussed and the usefulness of the table of derivs. below to differentiate among these compds. is emphasized. The following derivs. of VI, IX, VII, and Va were prepd. (m.p. given): hydrochloride, 320°, 286–8°, 265°, 262°; hydrobromide, 360°, 267°, 244°, 239°; hydriodide, above 360° (chars without melting), 231° (tri salt), 237°, 266° (di salt); methobromide, 296°, 296° (tri salt), 364° (evacuated tube) 315° (di salt); methiodide, 284°, 288° (di salt) (tri salt, m. 270°), 334° (sealed tube), 320° (di salt); methopicrate, 324°, 212° (tri salt), 320°, 220° (di salt); *p*-nitrophenoxide, 182–3°, 184°, 125–6°, 139°; 2,4-dinitrophenoxide, 158°, 221°, 216°, 165°; picrate, 290°, 292°, 300°, 254°; nitrate, 176°, 245°, 210°, 164°; oxalate, 290°, 239–40°, 276°, 228°; and chloroplatinate, 324°, 287°, 282°, 242°. VI was studied against an infection of *Heterakis spumosa* in mice. It shows no activity at doses of 1.25 g./kg. given three times. Piperazine is fully active at this dose level. VI produces no marked pharmacol. effects in the cat, except transient decrease in blood pressure. VI is also without action in cotton rats infected with *Litomosoides carinii* at a dose of 1 g./kg. IV and V are inactive as possible schistosomicides. Robert Filler

Electrophilic substitution X. Nitration of quinoxaline. M. J. S. Dewar and P. M. Maitlis (Univ. London). *J. Chem. Soc.* 1957, 2518–21; *C.A.* 51, 12091*g*.—Quinoxaline (I) was shown to be mononitrated in the 5-position (II) and dinitrated in the 5,6-positions (III). I (11 g.) in 50 ml. H_2SO_4 was added to a mixt. of 25 ml. HNO_3, 50 ml. H_2SO_4, and 50 ml. 65% oleum, the mixt. heated 24 hrs. at 85–90°, cooled, and hydrolyzed by pouring on ice, the solid extd. with $CHCl_3$-Me_2CO, and the ext. evapd. gave 12 g. tar, which purified gave 5.1 g. III, prisms, m. 172–3°. Evapn. of the mother liquors and chromatography of the residue gave 0.2 g. more III and 0.3 g. II, m. 95–6° as yellow needles. Only 0.4 g. of I was recovered by neutralizing the origina soln. $N_2H_4.H_2O$ (3 ml.) and 50 mg. Pd-C added at 70° to 0.9 g. III in alc., after 0.5 hr. the soln. filtered, the filtrate evapd., and the product warmed 5 min. with 10 m. Ac_2O and 0.1 ml. concd. H_2SO_4 gave 0.1 g. 5-acetamidoquinoxaline, m. 130–1°. III (0.95 g.) refluxed 0.5 hr. in AcOH with 1 g. Fe powder, and the product hydrolyzed, neutralized, and acetylated gave 0.25 g. 2′-methylglyoxalino[4′,5′:5,6]-quinoxaline (IV), m. 249–9.5°. The formation of IV suggested that the 2 original NO_2 groups were ortho to each other. The reduction was then repeated and the products sepd. at the amine stage by chromatography into a small amt. of IV and 0.2 g. diamine (V). Phenanthraquinone (0.15 g.) in 1 ml. AcOH warmed with 0.14 g. V in 1 ml. alc. gave 0.2 g. 1,2,3,4-dibenzopyrazino[2′,3′:6,7]phenazine (VI), m. above 300° (from $MeNO_2$). When the spectrum of VI compared with that of 1,2,3,4,5,6-tribenzanthrene, allowing for the difference in intensity of the various peaks, a bathochromic shift of about 13 mμ for the hydrocarbon made the spectra superimposable. Fe powder (0.5 g.) refluxed 0.5 hr. with 0.5 g. III, 3 ml. Ac_2O, and 2 ml. AcOH, and the product chromatographed on Al_2O_3 gave 0.45 g. 5,6-diacetamidoquinoxaline (VII), m. 232–3° (from aq. alc.). Attempts to hydrolyze VII failed. After heating 0.5 hr. with 5*N* HCl unchanged VII was recovered. Hydrolysis by 5*N* NaOH gave tars. I (1 g.) in 12 ml. $(CF_3CO)_2O$ and 0.5 ml. HNO_3 left 88 hrs. at room temp. gave 0.43 g. hydroxynitroquinoxaline, m. 182–3° (from Me_2CO), which did not correspond to any of the known isomers. **XI. Nitration of some six-membered N-heterocyclic compounds in sulfuric acid.** *Ibid.* 2521–8.—The proportions of mono-NO_2 derivs. formed from quinoline (I) and isoquinoline (II) in H_2SO_4 were detd. I gave at 0° 47.7% 5- (III) and 52.3% 8-nitroquinoline (IV); II gave 5- (V) and 8-nitroisoquinoline (VI) in the proportions: 90.4% V, 9.6% VI at 0°; 84.8% V and 15.2% VI at 100°. Both reactions took place readily under mild conditions. For II a value for the parameter α was derived from the partial rate factors and was used, together with a value for β, for predictions of the reactivities of different positions in several 6-membered heterocyclic systems, giving excellent agreement with expt. Competitive nitrations were also carried out with I-II and I-acridine (VII); their significance was discussed. The relative reactivities were: I:II = 1:24.5; I:VII = 1:190. Attempts to follow the kinetics failed because the reactions were essentially complete in less than 1 min. at 0°. The π-electron energy difference was calcd. from the equation: $\Delta E_\pi = 2\beta_{r'}(a_{or} + a_{os})$ where atoms r and s were those adjacent to the point of attack. The value for $\beta_{r'}$ was found to be −6 kcal./mole for nitration in Ac_2O and −4 kcal./mole for nitration in H_2SO_4. Thus it was shown that for a given reagent X, the velocity constant K_r was given by $\log K_r = A_x - (\Delta E_\pi)_1/RT$. Thus $\alpha = 39.7 \pm 2$ kcal./mole when calcd. from the above equations for VI. The theory broke down in only 2 cases; 1st, when the position being considered was ortho to the ring N atom (as the 8-position in I and the 1-position in VII); 2nd, for positions analogous to the 4-phenanthryl positions. The results for a series of calcns. on the following 6-membered heterocycles were listed: pyridine, I, II, quinoxaline, quinazoline, cinnoline, VII, phenanthridine, benzo[*f*]quinoline, phenazine, and benzo[*c*]cinnoline. From results the ratio of the partial rate factors $K_V:K_{III}$ was calcd. to be 46.4:1 and $\Delta E_{\pi(III)} - \Delta E_{\pi(V)}$ was found to be −1.3 kcal./mole. This gave a theoretical value for the ratio of these partial rate factors of 10.5:1. HNO_3 (6.2 ml.) heated 1 hr. at 95° with 18 g. isoquinoline *N*-oxide in 80 ml. H_2SO_4 gave 13 g. 5-nitroisoquinoline *N*-oxide, m. 220–1° (from $MeNO_2$), and chromatography of the mother liquors yielded 2.2 g. isoquinoline *N*-oxide and 1.4 g. 8-nitroisoquinoline *N*-oxide (VIII), m. 188–9°. VIII (0.5 g.) refluxed 0.5 hr. in 7 ml. PCl_3 gave 65% VI, m. 87–7.5°. Reduction of VI with $N_2H_4.H_2O$ and Pd-C gave 60% 8-aminoisoquinoline, yellow needles, m. 170–1° (from ligroine). V was prepd. from the *N*-oxide in an analogous manner in 52% yield. I and II were dissolved in H_2SO_4, a soln. of HNO_3 added gradually and after 0.5 hr. the solns. poured on ice. The mononitro fraction was sepd. by partial basification (at pH 2.1 for I; at pH 2.5 for II) from unchanged base and analyzed spectroscopically. With I, both III and IV had peaks around 300 mμ and troughs at 250 mμ, whereas the 3-, 6-, and 7-isomer had considerable peaks at 250 mμ. B. K. Wasson

Syntheses with bis(pyridinium salts); a new pathway to the phenazine series. Otto Westphal and Klaus Jann (A. Wander-Forschungsinst. Freiburg/Zähringen, Ger.). *Ann.* 605, 8–15(1957).—$(ClCH_2CH{:})_2$ (18 g.) in 50 cc. $PhCH_2OH$ and 40 cc. pyridine kept 3 days at 20° and treated with 50 cc. Me_2CO gave 32 g. $[(C_5H_5NCH_2CH{:})_2]2Cl$ (I), hygroscopic, m. 209–10°, 2.83 g. of which in 16 cc. 50% EtOH with 3.3 g. *p*-$ONC_5H_4NMe_2$ (II) in 35 cc. EtOH and 4.2 g. piperidine after several hrs. at 0° gave 3.05 g. [*p*-$Me_2NC_6H_4$-*N*(*O*):*CHCH*:]$_2$ (fumaraldehyde dinitrone), red microneedles and stars, m. 238° (decompn.) (from hot $PhNO_2$). I (1.5 g.) in 10 cc. 50% EtOH with 1 g. II in 20 cc. EtOH and 0.5 g. NaCN in 5 cc. H_2O at 20° gave 0.8 g. of the fumaraldehyde bis(cyanoanil), [*p*-$Me_2NC_6H_4N$:*C*(*CN*)*CH*:]$_2$, dark red needles, m. 330° (decompn.) (after washing with 50% EtOH), which were not recrystd. $(BrCH_2CO)_2$ (10.7 g.) in 40 cc. EtOH at 0° with 6 g. 1,2-$C_6H_4(NH_2)_2$ gave 12 g. *2,3-bis(bromomethyl)quinoxaline* (III), yellow needles, m. 150–1° (from EtOH). III (10 g.) in 50 cc. hot Me_2CO and 40 cc. EtOH added to 12 cc. pyridine gave 11.4 g. *quinoxaline 2,3-bis(methylenepyridinium bromide)* (IV), $C_{20}H_{18}N_4Br_2$, hexagons, m. 204–5° (from abs. EtOH); *dihydrate*, m. 264–5° (from aq. EtOH). IV (5 g.) in 30 cc. 50% EtOH treated with 3.8 g. II in 45 cc. EtOH, cooled to 10°, and 2.2 g. NaCN in 8 cc. H_2O added after further cooling gave almost quantitatively the corresponding *bis(cyanoanil)* of *2,3-quinoxaline dialdehyde*, $C_{22}H_{14}N_8$, red needles with coppery surface luster, decomp. about 226° (from pyridine). IV (1 g.) and 0.7 g. Ac_2 in 10 cc. EtOH at 0° treated with 0.9 cc. Bu_2NH and kept 2 days at 0° gave 570 mg. crude *1-amino-2,3-dimethylphenazine-4-pyridinium bromide dihydrate* (V), $C_{19}H_{17}N_4Br.2H_2O$, red microneedles, m. 304–5° (from H_2O), 400 mg. of which were refluxed 4 hrs. with 2.5 cc. pyridine, and, after 12 hrs. at 20°, washed with H_2O, dried, and sublimed at 180°/0.002, to give 200 mg. *1,4-diamino-2,3-dimethylphenazine* (VI), diamagnetic, dark blue-violet needles, decomp. about 215°, and giving a blue EtOH soln. which was decolorized by AcOAg with sepn. of Ag. VI (70 mg.) heated 5 min. with 3 cc. pyridine and 2 cc. Ac_2O gave almost quantitatively the *1,4-di-Ac deriv.* (VII) of VI, lemon-yellow needles, m. 333–4° (after sublimation at 270°/760). V (0.5 g.) refluxed 5 min. with 5 cc. pyridine